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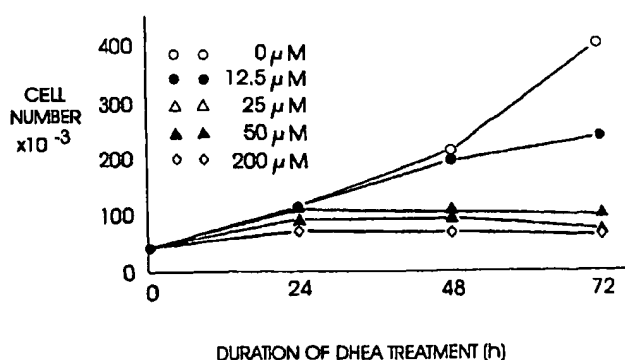
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(54) Title: COMPOSITIONS, FORMULATIONS AND KIT WITH ANTI-SENSE OLIGONUCLEOTIDE AND ANTI-INFLAMMATORY STEROID AND/OR UBIQUINONE FOR TREATMENT OF RESPIRATORY AND LUNG DISEASE



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(57) Abstract: A pharmaceutical composition and formulations comprise preventative, prophylactic or therapeutic amounts of an oligo(s) anti-sense to a specific gene(s) or its corresponding mRNA(s), and a glucocorticoid and/or non-glucocorticoid steroid or a ubiquinone or their salts. The agents, composition and formulations are used for treatment of ailments associated with impaired respiration, bronchoconstriction, lung allergy(ies) or inflammation, and abnormal levels of adenosine, adenosine receptors, sensitivity to adenosine, lung surfactant and ubiquinone, such as pulmonary fibrosis, vasoconstriction, inflammation, allergies, allergic rhinitis, asthma, impeded respiration, lung pain, cystic fibrosis, bronchoconstriction, COPD, RDS, ARDS, cancer, and others. The present treatment is effectively administered by itself for conditions without known therapies, as a substitute for therapies exhibiting undesirable side effects, or in combination with other treatments, e.g. before, during and after other respiratory system therapies, radiation, chemotherapy, antibody therapy and surgery, among others. Each of the agents of this invention may be administered directly into the respiratory system so that they gain direct access to the lungs, or by other effective routes of administration. A kit comprises a delivery device, the agents and instructions for its use.



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**COMPOSITIONS, FORMULATIONS & KIT WITH ANTI-SENSE  
OLIGONUCLEOTIDE & ANTI-INFLAMMATORY STEROID AND/OR UBIQUINONE  
FOR TREATMENT OF RESPIRATORY & LUNG DISEASE**

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**BACKGROUND OF THE INVENTION**

**Field of the Invention**

This invention concerns itself with compositions, formulations and kits employed for the administration of active agents that are effective for treating respiratory and pulmonary diseases including bronchoconstriction, impaired airways, decreased lung surfactant, asthma, rhinitis, acute respiratory distress syndrome (ARDS), infantile or maternal RDS, chronic obstructive pulmonary disease (COPD), allergies, impeded respiration, lung pain, cystic fibrosis (CF), infectious diseases, cancers such as leukemias, lung and colon cancer, and the like, and diseases whose secondary effects afflict the lungs. The active agents, anti-sense oligonucleotides and steroid agents and/or ubiquinones may be administered preventatively, prophylactically or therapeutically as a single therapy or in conjunction with other therapies.

**Background of the Invention**

Respiratory ailments, associated with a variety of diseases and conditions, are extremely common in the general population, and more so in certain ethnic groups, such as African Americans. In some cases they are accompanied by inflammation, which aggravates the condition of the lungs. Asthma, for example, is one of the most common diseases in industrialized countries. In the United States it accounts for about 1% of all health care costs. An alarming increase in both the prevalence and mortality of asthma over the past decade has been reported, and asthma is predicted to be the preeminent occupational lung disease in the next decade. While the increasing mortality of asthma in industrialized countries could be attributable to the depletion reliance upon beta agonists in the treatment of this disease, the underlying causes of asthma remain poorly understood. Respiratory and pulmonary diseases such as asthma, allergic rhinitis, Acute Respiratory Distress Syndrome (ARDS), including that occurring in pregnant mothers and in premature born infants, pulmonary fibrosis, cystic fibrosis (CF), chronic obstructive pulmonary disease (COPD), and cancer, among others, are common diseases in industrialized countries. In the United States alone they account for extremely high health care costs, and their incidence has recently been increasing at an alarming rate, both in terms of prevalence, morbidity and mortality. In spite of this, their underlying causes still remain poorly understood.

Asthma is a condition characterized by variable, in many instances reversible obstruction of the airways. This process is associated with lung inflammation and in some cases lung allergies. Many patients have acute episodes referred to as "asthma attacks," while others are afflicted with a chronic condition. The asthmatic process is triggered in some cases by inhalation of antigens by hypersensitive subjects. This condition is generally referred to as "extrinsic asthma." Other asthmatics have an intrinsic predisposition to the condition, which is thus referred to as "intrinsic asthma," and may be comprised of conditions of different origin, including those mediated by the adenosine receptor(s), allergic conditions mediated by an immune IgE-mediated response, and others. All asthmas have a group of symptoms, which are characteristic of this condition: bronchoconstriction, lung inflammation and decreased lung surfactant. Existing bronchodilators and anti-inflammatories are currently commercially available and are prescribed for the treatment of asthma. The most common anti-inflammatories, corticosteroids, have considerable side effects but are commonly prescribed nevertheless. Most of the drugs available for the treatment of asthma are, more importantly, barely effective in a small number of patients.

Acute Respiratory Distress Syndrome (ARDS), or stiff lung, shock lung, pump lung and congestive atelectasis, is believed to be caused by fluid accumulation within the lung which, in turn, causes the lung to stiffen. The condition is triggered within 48 hours by a variety of processes that injure the lungs such as trauma, head injury, shock, sepsis, multiple blood transfusions, medications, pulmonary embolism, severe pneumonia, smoke inhalation, radiation, high altitude, near drowning, and others. In general, ARDS occurs as a medical emergency and may be caused by other conditions that directly or indirectly cause the blood vessels to "leak" fluid into the lungs. In ARDS, the ability of the lungs to expand is severely decreased and produces extensive damage to the air sacs and lining or endothelium of the lung. ARDS' most common symptoms are labored, rapid breathing, nasal flaring,

5 cyanosis blue skin, lips and nails caused by lack of oxygen to the tissues, breathing difficulty, anxiety, stress, tension, joint stiffness, pain and temporarily absent breathing. ARDS is commonly diagnosed by testing for symptomatic signs, for example by a simple chest auscultation or examination with a stethoscope that may reveal abnormal symptomatic breath sounds. A preliminary diagnosis of ARDS may be confirmed with chest X-rays and the measurement of arterial blood gas. In some cases ARDS appears to be associated with other diseases, such as acute myelogenous leukemia, with acute tumor lysis syndrome (ATLS) developed after treatment with, e.g. cytosine arabinoside. In general, however, ARDS appears to be associated with traumatic injury, severe blood infections such as sepsis, or other systemic illness, high dose radiation therapy and chemotherapy, and inflammatory responses which lead to multiple organ failure, and in many cases death. In premature babies ("premies"), the lungs are not quite developed and, therefore, the fetus is in an anoxic state during development. Moreover, lung surfactant, a material critical for normal respiration, is generally not yet present in sufficient amounts at this early stage of life; however, premies often hyper-express the adenosine A<sub>1</sub> receptor and/or underexpress the adenosine A<sub>2a</sub> receptor and are, therefore, susceptible to respiratory problems including bronchoconstriction, lung inflammation and ARDS, among others. When Respiratory Distress Syndrome (RDS) occurs in premies, it is an extremely serious problem. Preterm infants exhibiting RDS are currently treated by ventilation and administration of oxygen and surfactant preparations. When premies survive RDS, they frequently develop bronchopulmonary dysplasia (BPD), also called chronic lung disease of early infancy, which is often fatal.

The systemic administration of adenosine was found useful for treating SVT, and as a pharmacologic means to evaluate cardiovascular health via an adenosine stress test commonly administered by hospitals and by doctors in private practice. Adenosine administered by inhalation, however, is known to cause bronchoconstriction in asthmatics, possibly due to mast cell degranulation and histamine release, effects which have not been observed in normal subjects. Adenosine infusion has caused respiratory compromise, for example, in patients with COPD. As a consequence of the untoward side effects observed in many patients, caution is recommended in the prescription of adenosine to patients with a variety of conditions, including obstructive lung disease, emphysema, bronchitis, etc, and complete avoidance of its administration to patients with or prone to bronchoconstriction or bronchospasm, such as asthma. In addition, the administration of adenosine must be discontinued in any patient who develops severe respiratory difficulties. It would be of great help if a formulation were to be made available for joint use when adenosine administration is required.

Allergic rhinitis afflicts one in five Americans, accounting for an estimated \$4 to 10 billion in health care costs each year, and occurs at all ages. Because many people mislabel their symptoms as persistent colds or sinus problems, allergic rhinitis is probably underdiagnosed. Typically, IgE combines with allergens in the nose to produce chemical mediators, induction of cellular processes, and neurogenic stimulation, causing an underlying inflammation. Symptoms include nasal congestion, discharge, sneezing, and itching, as well as itchy, watery, swollen eyes. Over time, allergic rhinitis sufferers often develop sinusitis, otitis media with effusion, and nasal polyposis that may exacerbate asthma, and is associated with mood and cognitive disturbances, fatigue and irritability. Degranulation of mast cells results in the release of preformed mediators that interact with various cells, blood vessels, and mucous glands to produce the typical rhinitis symptoms. Most early- and late-phase reactions occur in the nose after allergen exposure. The late-phase reaction is seen in chronic allergic rhinitis, with hypersecretion and congestion as the most prominent symptoms. Repeated exposure may cause hypersensitivity to one or many allergens. Sufferers may also become hyperreactive to non-specific triggers, such as cold air or strong odors. Non-allergic rhinitis may be induced by infections, such as viral infections, or associated with nasal polyps, as occurs in patients with aspirin idiosyncrasy. In addition, pregnancy, hypothyroidism, and exposure to occupational factors or medications may cause rhinitis, as well. NARES syndrome, a non-allergic type of rhinitis associated with eosinophils in nasal secretions, typically occurs in middle-aged individuals and is accompanied by loss of smell. Saline is often recommended to improve nasal stuffiness, sneezing, and congestion, since saline sprays usually relieve mucosal irritation or dryness associated with various nasal conditions, minimize mucosal atrophy, and dislodge encrusted or thickened mucus, while causing no side effects, and may be used freely in pregnant patients. In addition, if used immediately before intra-nasal corticosteroid dosing, saline helps prevent local irritation. Anti-histamines often serve as a primary therapy. Terfenadine and astemizole, two non-sedating anti-histamines, however, have been associated with a ventricular arrhythmia known as Torsades de Points, usually in interaction with other medications such as ketoconazole and erythromycin, or secondary to an underlying cardiac problem. Up to date, loratadine, another non-sedating anti-histamine, and cetirizine have not been associated with

serious adverse cardiovascular events. Cetirizine's most common side effect, however, is drowsiness. Claritin, for example, may be effective in relieving sneezing, runny nose, and nasal, ocular and palatal itching in a low percentage of patients, although not approved for this indication or asthma. Anti-histamines are typically combined with a decongestant to help relieve nasal congestion. Sympathomimetic medications are used as vasoconstrictors and decongestants, the most common being pseudoephedrine, phenylpropanolamine and phenylephrine. These agents, however, often cause hypertension, palpitations, tachycardia, restlessness, insomnia and headache. Topical decongestants are recommended for limited periods because their overuse results in nasal dilatation. Anti-cholinergic agents, such as cromolyn, have a role in patients with significant rhinorrhea or in specific cases, such as "gustatory rhinitis", which is usually associated with ingestion of spicy foods, and have been used on the common cold. Sometimes the Cromolyn spray produces sneezing, transient headache, and even nasal burning. Topical and nasal spray corticosteroids such as Vancenase are effective agents in the treatment of rhinitis, especially for symptoms of congestion, sneezing and runny nose, but sometimes may cause irritation, stinging, burning, sneezing, and local bleeding. Topical steroids are generally more effective than Cromolyn sodium, particularly in the treatment of NARES, but side effects sometimes limit their usefulness. Immunotherapy, while expensive and inconvenient, often provides substantial benefits, especially the use of drugs such as blocking antibodies, and those that alter cellular histamine release, and result in decreased IgE. Presently available treatments, such as propranolol, verapamil, and adenosine, may help to minimize symptoms. Verapamil is most commonly used but it has several shortcomings, since it causes or exacerbates systemic hypotension, congestive heart failure, bradyarrhythmias, and ventricular fibrillation. Verapamil, however, crosses the placenta and has been shown to cause fetal bradycardia, heart block, depression of contractility, and hypotension. Adenosine has several advantages over verapamil, including rapid onset, brevity of side effects, theoretical safety, and probable lack of placental transfer, but may not be administered to a variety of patients.

Chronic obstructive pulmonary disease (COPD) is characterized by airflow obstruction that is generally caused by chronic bronchitis, emphysema, or both. Emphysema is characterized by abnormal permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis. Chronic bronchitis is characterized by chronic cough, mucus production, or both, for at least three months for at least two successive years where other causes of chronic cough have been excluded. COPD characteristically affects middle aged and elderly people, and is one of the leading causes of morbidity and mortality worldwide. In the United States it affects about 14 million people and is the fourth leading cause of death, and both its morbidity and mortality rates are still rising. This contrasts with the decline over the same period in age-adjusted mortality from all causes, and from cardiovascular diseases. COPD, however, is preventable, since it is believed that its main cause is exposure to cigarette smoke. The disease is rare in lifetime non-smokers, in whom exposure to environmental tobacco smoke will explain at least some of the airways obstruction. Other proposed etiological factors include airway hyper-responsiveness or hypersensitivity, ambient air pollution, and allergy. The airflow obstruction in COPD is usually progressive in people who continue to smoke. This results in early disability and shortened survival time. Stopping smoking reverts the decline in lung function to values for non-smokers. Many patients will use medication chronically for the rest of their lives, with the need for increased doses and additional drugs during exacerbations. Amongst the currently available treatments for COPD, short-term benefits were found, as opposed to long term effects on progression, from anti-cholinergic drugs,  $\beta_2$  adrenergic agonists, and oral steroids. The effects of anti-cholinergic drugs and  $\beta_2$  adrenergic agonists, however, are not seen in all people with COPD, and the two agents combined are only slightly more effective than either alone. Their adverse effects and the need for frequent monitoring of blood concentrations limit the usefulness of theophyllines. There is no evidence that anti-cholinergic agents affect the decline in lung function, and mucolytics have been shown to reduce the frequency of exacerbations but with a possible deleterious effect on lung function. The long-term effects of  $\beta_2$  adrenergic agonists, oral corticosteroids, and antibiotics have not yet been evaluated, and up to the present time no other drug has been shown to affect the progression of the disease or survival. Thus, there is very little currently available to alleviate symptoms of COPD, prevent exacerbations, preserve optimal lung function, and improve daily living activities an quality of life. Thus, there is very little currently available to alleviate symptoms of COPD, prevent exacerbations, preserve optimal lung function, and improve daily living activities an quality of life.

Interstitial lung disease (ILD), interstitial pulmonary fibrosis, or simply pulmonary fibrosis are terms that include more than 130 chronic lung disorders that affect the lung in at least three ways: lung tissue is damaged in some known or unknown way, walls of the air sacs in the lung become inflamed, and scarring or fibrosis begins in

the interstitium (or tissue between the air sacs), and the lung becomes stiff. Breathlessness during exercise may be one of the first symptoms of these diseases, and a dry cough may be present. Neither the symptoms nor X rays are often sufficient to tell apart different types of pulmonary fibrosis. Some pulmonary fibrosis patients have known causes and some have unknown or idiopathic causes. Interstitial lung disease (or pulmonary fibrosis) is named after the tissue between the air sacs of the lungs because this is the tissue affected by fibrosis or scarring. The course of this disease is generally unpredictable. If they progress the lung tissue thickens and becomes stiff, breathing becomes more difficult and demanding, and inflammation occurs. Some people may need oxygen therapy as part of their treatment.

Microbial infections are extremely common, and may be caused by viruses, bacteria, and other forms of life. They are generally treated with anti-viral agents, antibiotics, and other specific therapeutic drugs. However, some infectious may either go unnoticed, or produce secondary effects such as inflammation, pulmonary and airway obstructions, and other pulmonary ailments.

Cancer is one of the most prevalent and feared diseases of our times. It generally results from the carcinogenic transformation of normal cells of different epithelia. Two of the most damaging characteristics of carcinomas and other types of malignancies are their uncontrolled growth and their ability to create metastases in distant sites of the host, particularly a human host. It is usually these distant metastases that cause serious consequences to the host, since frequently the primary carcinoma may be, in most cases, removed by surgery. The treatment of cancer presently relies on surgery, irradiation therapy and systemic therapies such as chemotherapy, different immunity-boosting medicines and procedures, hyperthermia and systemic, radioactively labeled monoclonal antibody treatment, immunotoxins and chemotherapeutic drugs.

Adenosine may constitute an important mediator in the lung for various diseases, including bronchial asthma, COPD, CF, RDS, rhinitis, pulmonary fibrosis, and others. Its potential role was suggested by the finding that asthmatics respond favorably to aerosolized adenosine with marked bronchoconstriction whereas normal individuals do not. An asthmatic rabbit animal model, the dust mite allergic rabbit model for human asthma, responded in a similar fashion to aerosolized adenosine with marked bronchoconstriction whereas non-asthmatic rabbits showed no response. More recent work with this animal model suggested that adenosine-induced bronchoconstriction and bronchial hyperresponsiveness in asthma may be mediated primarily through the stimulation of adenosine receptors. Adenosine has also been shown to cause adverse effects, including death, when administered therapeutically for other diseases and conditions in subjects with previously undiagnosed hyper reactive airways.

Adenosine is a purine involved in intermediary metabolism, and may constitute an important natural mediator of many of diseases. Adenosine plays a unique role in the body as a regulator of cellular metabolism. It can raise the cellular level of AMP, ADP and ATP which are the energy intermediates of the cell. Adenosine can stimulate or down regulate the activity of adenylate cyclase and hence regulate cAMP levels. cAMP, in turn, plays a role in neurotransmitter release, cellular division and hormone release. Adenosine's major role appears to be to act as a protective injury autocoid. In any condition in which ischemia, low oxygen tension or trauma occurs adenosine appears to play a role. Defects in synthesis, release, action and/or degradation of adenosine have been postulated to contribute to the over activity of the brain excitatory amino acid neurotransmitters, and hence various pathological states. Adenosine has also been implicated as a primary determinant underlying the symptoms of bronchial asthma and other respiratory diseases, the induction of bronchoconstriction and the contraction of airway smooth muscle. Moreover, adenosine causes bronchoconstriction in asthmatics but not in non-asthmatics. Other data suggest the possibility that adenosine receptors may also be involved in allergic and inflammatory responses by reducing the hyperactivity of the central dopaminergic system. It has been postulated that the modulation of signal transduction at the surface of inflammatory cells influences acute inflammation. Adenosine is said to inhibit the production of super-oxide by stimulated neutrophils. Recent evidence suggests that adenosine may also play a protective role in stroke, CNS trauma, epilepsy, ischemic heart disease, coronary by-pass, radiation exposure and inflammation. Overall, adenosine appears to regulate cellular metabolism through ATP, to act as a carrier for methionine, to decrease cellular oxygen demand and to protect cells from ischemic injury. Adenosine is a tissue hormone or inter-cellular messenger that is released when cells are subject to ischemia, hypoxia, cellular stress, and increased workload, and or when the demand for ATP exceeds its supply. Adenosine is a purine and its formation is directly linked to ATP catabolism. It appears to modulate an array of physiological processes including vascular tone, hormone action, neural function, platelet aggregation and lymphocyte differentiation. It also may play a role in

DNA formation, ATP biosynthesis and general intermediary metabolism. It is suggested that it regulates the formation of cAMP in the brain and in a variety of peripheral tissues. Adenosine regulates cAMP formation through two receptors A<sub>1</sub> and A<sub>2</sub>. Via A<sub>1</sub> receptors, adenosine reduces adenylate cyclase activity, while it stimulates adenylate cyclase at A<sub>2</sub> receptors. The adenosine A<sub>1</sub> receptors are more sensitive to adenosine than the A<sub>2</sub> receptors.

5 The CNS effects of adenosine are generally believed to be A<sub>1</sub>-receptor mediated, where as the peripheral effects such as hypotension, bradycardia, are said to be A<sub>2</sub> receptor mediated.

Anti-sense oligonucleotides have received considerable theoretical consideration as potential useful pharmacological agents in human disease. One important impediment to their effective application has been a difficulty in finding an appropriate route of administration to deliver them to their site of action. The administering

10 of anti-sense oligonucleotides directly to specific regions of the brain, for example, necessarily has limited clinical utility due to its invasive nature. Finding practical and effective applications for these agents in actual models of human disease have been few and far between, particularly because they had to be administered in large doses. The systemic administration of anti-sense oligonucleotides as pharmacological agents, such as oral and parenteral administration, has been found to have also significant problems, including the inherent difficulty in targeting

15 specific tissues due to their dilution in the circulatory system. The bioavailability of orally administered anti-sense oligonucleotides is very low, of the order of less than about 5%. The present inventor previously pioneered the administration of oligonucleotides via the respiratory system, and successfully treated asthma, bronchoconstriction and lung inflammation and allergies, and applied the technology to the treatment of other conditions. The route of administration, thus was found to be of importance, particularly for treating localized conditions. As described in

20 more detail below, the lung is an excellent target for the direct administration of anti-sense oligonucleotides and provides a non-invasive and a tissue-specific route. The respiratory system, and in particular the lung, as the ultimate port of entry into the organism provides an excellent route of administration for anti-sense oligonucleotides. This is so not only for the treatment of lung disease, but also when utilizing the lung as a means for delivery, particularly because of its non-invasive and tissue-specific nature. Thus, local delivery of anti-sense oligos directly

25 to the target tissue enables an optimal delivery for the therapeutic use of these compounds. Fomivirsen (ISIS 2922) is an example of a local drug delivery into the eye to treat cytomegalovirus (CMV) retinitis, for which a new drug application has been filed by ISIS. The administration of a drug through the lung offers the further advantage that inhalation is non-invasive whereas direct injection into the vitreous of the eye is invasive.

Steroids are naturally occurring compounds of varied activities. In mammals, they serve different functions, some being associated with sexual cycles and reproduction, others with regulation of endogenous levels of various compounds. Some of these have anti-inflammatory activity,

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Steroid hormones are potent chemical messengers that exert dramatic effects on cell differentiation, homeostasis, and morphogenesis. These molecules diverse in structure share a mechanistically similar mode of action. The effector molecules diffuse across cellular membranes and bind to specific high affinity receptors in the

35 target cell nuclei. This interaction results in the conversion of an inactive receptor to one that can interact with the regulatory regions of target genes and modulate the rate of transcription of specific gene sets. Upon ligand binding, these receptors generate both rapid and long lasting responses. Steroids can act through two basic mechanisms: genomic and non-genomic. The classical genomic action is mediated by specific intracellular receptors, whereas the primary target for the non-genomic one is the cell membrane. Many clinical symptoms seem to be mediated

40 through the non-genomic route. Furthermore, membrane effects of steroid and other factors can interfere with the intranuclear receptor system inducing or repressing steroid-and receptor-specific genomic effects. These signalling pathways may lead to unexpected hormonal or anti-hormonal effects in patients treated with certain drugs.

Steroid receptors are members of a large family of nuclear transcription factors that regulate gene expression by binding to their cognate steroid ligands, to the specific enhancer sequences of DNA (steroid response

45 elements) and to the basic transcription machinery. Steroid receptors are basically localized in the nucleus, regardless of hormonal status, and considerable-amounts of unliganded steroid receptors may be present in the cytoplasm of target cells in exceptional cases. Most steroid receptors are phosphoproteins, which are further phosphorylated after ligand binding. The role of phosphorylation in receptor transduction is complex and may not be uniform to all steroid receptors. However, phosphorylation and/or dephosphorylation is believed to be a key event

50 regulating the transcriptional activity of steroid receptors. Steroid receptor activities can be affected by the amount of steroid receptor in the cell nuclei, which is modified by the rate of transcription and translation of the steroid receptor gene as well as by proteolysis of the steroid receptor protein. There is an auto- and heteroregulation of

receptor levels. Some of the steroid receptors appear to bind specific protease inhibitors and exhibit protease activity. Some steroid receptors are expressed as two or more isoforms, which may have different effects on transcription. Receptor isoforms are different translation or transcription products of a single gene. Isoform A of the progesterone receptor is a truncated form of PR isoform B originating from the same gene, but it is able to suppress not only the gene enhancing activity of PR-B but also that of other steroid receptors.

Before hormone binding, the receptors are part of a complex with multiple chaperones which maintain the receptor in its steroid binding conformation. Following hormone binding, the complex dissociates and the receptors bind to steroid response elements in chromatin. Regulation of gene expression by hormones involves an interaction of the DNA-bound receptors with other sequence-specific transcription factors and with the general transcription factors, which is partly mediated by co-activators and co-repressors. The specific array of cis regulatory elements in a particular promoter/enhancer region, as well as the organization of the DNA sequences in nucleosomes, specifies the network of receptor interactions. Depending on the nature of these interactions, the final outcome can be induction or repression of transcription.

Adrenocortical hormones are steroid hormones classified as glucocorticoids, mineralocorticoids and sex hormones. Glucocorticoids moderate the metabolism of sugar, fat and protein and may raise the resistance to the adverse stimulation of the body by these substances. Many of the clinically useful steroids belong to this group, including cortisone, hydrocortisone, and their pharmaceutical derivatives such as prednisone, dexamethasone, etc. Although glucocorticoids were originally so called because of their influence on glucose metabolism, they are currently defined as steroids that exert their effects by binding to specific cytosolic receptors that mediate the actions of these hormones. These glucocorticoid receptors are present in virtually all tissues, and glucocorticoid-receptor interactions are responsible for most of the known effects of these steroids. Alteration in the structure of these glucocorticoids has led to the development of synthetic compounds with greater glucocorticoid activity. The increased activity of these compounds is due to increased affinity for the glucocorticoid receptors and/or delayed plasma clearance, which increases tissue exposure. In addition, many of these synthetic glucocorticoids evidence negligible mineralocorticoid effects and thus do not result in sodium retention, hypertension, and/or hypokalemia. Glucocorticoid action is initiated by entry of the steroid into the cell and binding to the cytosolic glucocorticoid receptor proteins. After binding, activated hormone-receptor complexes enter the nucleus and interact with nuclear chromatin acceptor sites. These events cause the expression of specific genes and the transcription of specific mRNAs. The resulting proteins affect the response to the glucocorticoids, which may be inhibitory or stimulatory depending on the specific tissue affected. Although glucocorticoid receptors are similar in many tissues, the proteins synthesized vary widely and are the result of expression of specific genes in different cell types.

Mineralocorticoids and sex hormones are non-glucocorticoid steroids, e.g., adrenal androgens. Adrenal androgens, such as androstenediones, dehydroepiandrosterone (DHEA), and DHEA sulfate function as precursors for the peripheral conversion to androgenic hormones, such as testosterone and dihydrotestosterone. DHEA sulfate secreted by the adrenal undergoes limited conversion to DHEA, and both the peripheral DHEA and DHEA secreted by the adrenal cortex may be further converted in peripheral tissues to androstenedione, the immediate precursor of the active androgens. Dehydroepiandrosterone (DHEA) is a naturally occurring steroid secreted by the adrenal cortex with apparent chemoprotective properties. Epidemiological studies have shown that low endogenous levels of DHEA correlate with increased risk of developing some forms of cancer, such as pre-menopausal breast cancer in women and bladder cancer in both sexes. The ability of DHEA and DHEA analogues, e.g. dehydroepiandrosterone sulfate (DHEA-S), to inhibit carcinogenesis is believed to result from their uncompetitive inhibition of the activity of the enzyme glucose 6-phosphate dehydrogenase (G6PDH). G6PDH is the rate limiting enzyme of the hexose monophosphate pathway, a major source of intracellular ribose-5-phosphate and NADPH. Ribose-5 phosphate is a necessary substrate for the synthesis of both ribo- and deoxyribonucleotides required for the synthesis of RNA and DNA. NADPH is a cofactor also involved in nucleic acid biosynthesis and the synthesis of hydroxymethylglutaryl Coenzyme A reductase (HMG CoA reductase). HMG CoA reductase is an unusual enzyme that requires two moles of NADPH for each mole of product, mevalonate, produced. Thus, it appears that HMG CoA reductase would be ultrasensitive to DHEA-mediated NADPH depletion, and that DHEA-treated cells would rapidly show the depletion of intracellular pools of mevalonate. Mevalonate is required for DNA synthesis, and DHEA arrests human cells in the G1 phase of the cell cycle in a manner closely resembling that of the direct HMG CoA. Because G6PDH produces mevalonic acid used in cellular processes such as protein isoprenylation and the synthesis of dolichol, a precursor for glycoprotein biosynthesis, DHEA inhibits carcinogenesis by depleting mevalonic acid and thereby

inhibiting protein isoprenylation and glycoprotein synthesis. Mevalonate is a central precursor for the synthesis of cholesterol, as well as for the synthesis of a variety of non-sterol compounds involved in post-translational modification of proteins, such as farnesyl pyrophosphate and geranyl pyrophosphate. Mevalonate is also a central precursor for the synthesis of dolichol, a compound that is required for the synthesis of glycoproteins involved in cell-to-cell communication and cell structure. Mevalonate is also central to the manufacture of ubiquinone, an antioxidant with an established role in cellular respiration. It has long been known that patients receiving steroid hormones of adrenocortical origin at pharmacologically appropriate doses show increased incidence of infectious disease.

DHEA, also known as  $3\beta$ -hydroxyandrost-5-en-17-one or dehydroepiandrosterone, is a 17-ketosteroid which is quantitatively one of the major adrenocortical steroid hormones found in mammals. Although DHEA appears to serve as an intermediary in gonadal steroid synthesis, the primary physiological function of DHEA has not been fully understood. It has been known, however, that levels of this hormone begin to decline in the second decade of life, reaching 5% of the original level in the elderly.) Clinically, DHEA has been used systemically and/or topically for treating patients suffering from psoriasis, gout, hyperlipemia, and it has been administered to post-coronary patients. In mammals, DHEA has been shown to have weight optimizing and anti-carcinogenic effects, and it has been used clinically in Europe in conjunction with estrogen as an agent to reverse menopausal symptoms and also has been used in the treatment of manic depression, schizophrenia, and Alzheimer's disease. DHEA has also been used clinically at 40 mg/kg/day in the treatment of advanced cancer and multiple sclerosis. Mild androgenic effects, hirsutism, and increased libido were the side effects observed. These side effects can be overcome by monitoring the dose and/or by using analogues. The subcutaneous or oral administration of DHEA to improve the host's response to infections is known, as is the use of a patch to deliver DHEA. DHEA is also known as a precursor in a metabolic pathway that ultimately leads to more powerful agents that increase immune response in mammals. That is, DHEA acts as a biphasic compound: it acts as an immuno-modulator when converted to androstenediol or androst-5-ene- $3\beta$ , $17\beta$ -diol ( $\beta$ AED), or androstenediol or androst-5-ene- $3\beta$ , $7\beta$ , $17\beta$ -triol ( $\beta$ AET). However, in vitro DHEA has certain lymphotoxic and suppressive effects on cell proliferation prior to its conversion to  $\beta$ AED and/or  $\beta$ AET. It is, therefore, believed that the superior immunity enhancing properties obtained by administration of DHEA result from its conversion to more active metabolites.

Adequate ubiquinone levels have been found to be essential for maintaining proper cardiac function, and the administration of exogenous ubiquinone has recently been shown to have beneficial effect in patients with chronic heart failure. Ubiquinone depletion has been observed in humans and animals treated with lovastatin, a direct HMG CoA reductase inhibitor. Such lovastatin-induced depletion of ubiquinone has been shown to lead to chronic heart failure, or to a shift from low heart failure into life-threatening high grade heart failure. DHEA, unlike lovastatin, inhibits HMG CoA reductase indirectly by inhibiting G6PDH and depleting NADPH, a required cofactor for HMG CoA reductase. However, DHEA's indirect inhibition of HMG CoA reductase suffices to deplete intracellular mevalonate. This effect adds to the depletion of ubiquinone, and may result in chronic heart failure following long term usage. Thus, although DHEA was once considered a safe drug, it is now predicted that with long term administration of DHEA or its analogues, chronic heart failure may occur as a complicating side effect. Further, some analogues of DHEA produce this side effect to a greater extent because, in general, they are more potent inhibitors of G6PDH than DHEA.

A handful of medicaments have been used for the treatment of respiratory diseases and conditions, although in general they all have limitations. Amongst them are corticoid steroids with glucocorticoid activity, leukotriene inhibitors, anti-cholinergic agents, anti-histamines, oxygen therapy, theophyllines, and mucolytics. Corticosteroids are the ones with the most widespread use in spite of their well documented side effects. Most of the available drugs are nevertheless effective in a small number of cases, and not at all when it comes to the treatment of asthma. No treatments are currently available for many of the other respiratory diseases. Theophylline, an important drug in the treatment of asthma, is a known adenosine receptor antagonist that was reported to eliminate adenosine-mediated bronchoconstriction in asthmatic rabbits. A selective adenosine  $A_1$  receptor antagonist, 8-cyclopentyl-1, 3-dipropylxanthine (DPCPX) was also reported to inhibit adenosine-mediated bronchoconstriction and bronchial hyperresponsiveness in allergic rabbits. The therapeutic and preventative applications of currently available adenosine  $A_1$  receptor-specific antagonists are, nevertheless, limited by their toxicity. Theophylline, for example, has been widely used in the treatment of asthma, but is associated with frequent, significant toxicity resulting from its narrow therapeutic dose range. DPCPX is far too toxic to be useful clinically. The fact that, despite decades of



extensive research, no specific adenosine receptor antagonist is available for clinical use attests to the general toxicity of these agents.

For many years, two classes of compounds have dominated the treatment of asthma: corticosteroids having glucocorticoid activity and bronchodilators. Examples of corticosteroids are beclomethasone and corticoid 21-sulfopropionates. Examples of a bronchodilator are an older  $\beta_2$  adrenergic agonist such as albuterol, and a newer one such as salmeterol. In general, when glucocorticosteroids are taken daily either by inhalation or orally, they attenuate inflammation. The  $\beta_2$  adrenergic agonists, on the other hand, primarily alleviate bronchoconstriction. Whereas glucocorticosteroids are not useful in general for acute settings, bronchodilators are used in acute care, such as in the case of asthma attacks. At the present time, many asthma patients require daily use of both types of agents, a glucocorticosteroid to contain pulmonary inflammation, and a bronchodilator to alleviate bronchoconstriction. More recently, fluticasone propionate, a corticosteroid was combined with  $\beta_2$  adrenergic agonists in one therapeutic formulation said to have greater efficiency in the treatment of asthma. However, glucocorticosteroids, particularly when taken for prolonged periods, have extremely deleterious side effects that, although somewhat effective, make their chronic use undesirable, particularly in children.

Clearly, there exists a well defined need for novel and effective therapies for treating respiratory, lung and cancer ailments that cannot presently be reasonably treated, or at least for which no therapies are available that are effective and devoid of significant detrimental side effects. Moreover, there is a definite need for treatments that have prophylactic and therapeutic applications, and require low amounts of active agents, and are less costly and less prone to detrimental side effects. Furthermore, it is readily apparent that anti-inflammatory steroids ("AIS"), including adrenal androgens, androgens and their derivatives, etc, corticoid and non-glucocorticoid steroids, ubiquinones and their respective salts, as well as specifically targeted anti-sense oligonucleotides (oligos) are each alone useful for the treatment of respiratory, lung, and cancer. This patent provides their joint effects that evidence unexpected superior results over each agent alone.

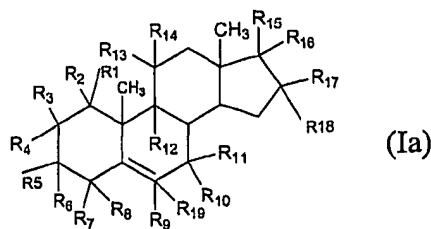
#### SUMMARY OF THE INVENTION

The present invention generally relates to a pharmaceutical or veterinary composition, comprising a pharmaceutically or veterinarily acceptable carrier or diluent, and first and second active agents.

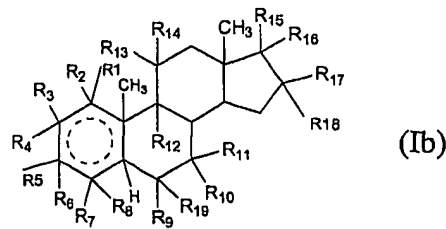
The first active agent comprises an oligonucleotide(s) (oligo(s)) that may be anti-sense to one or more targets, and a second active agent comprising anti-inflammatory steroids ("AIS") and/or a ubiquinone, in amounts effective for alleviating airway, lung, and microbial and/or cancer diseases associated with, for example, bronchoconstriction, impeded respiration, dyspnea, emphysema, asthma, COPD, ARDS, CF, allergic rhinitis, pulmonary hypertension and fibrosis, lung inflammation, allergies, surfactant depletion or hyposecretion, and cancers, among others. The oligo preferably contains about 0 to about 15% adenosine (A) and is anti-sense to the initiation codon, the coding region, the 5'-end or the 3'-end genomic flanking regions, the 5' or 3' intron-exon junctions, or regions within 2 to 10 nucleotides of the junctions of at least one gene regulating or encoding a target polypeptide associated with lung or airway dysfunction or cancer, or that is anti-sense to the corresponding mRNA, and the composition may comprise also combinations or mixtures of the oligos. The targets are typically molecules associated with airway disease, cancer, etc., such as transcription factors, stimulating and activating peptide factors, cytokines, cytokine receptors, chemokines, chemokine receptors, adenosine receptors, bradykinin receptors, endogenously produced specific and non-specific enzymes, immunoglobulins and antibodies, antibody receptors, central nervous system (CNS) and peripheral nervous and non-nervous system receptors, CNS and peripheral nervous and non-nervous system peptide transmitters, adhesion molecules, defensins, growth factors, vasoactive peptides and receptors, binding proteins, and malignancy associated proteins, among others. In one embodiment the first active agent comprises a nucleic acid wherein the oligo is anti-sense to more than one target. These are called within the four corners of this patent multiple target anti-sense oligonucleotides or MTAs.

The second active agent comprises an anti-inflammatory steroid such as an adrenal androgen of the chemical formula





or



wherein  $R_1, R_2, R_3, R_4, R_6, R_7, R_8, R_9, R_{10}, R_{12}, R_{13}, R_{14}$  and  $R_{19}$  are independently H, OR, halogen,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkyne,  $(C_1-C_{10})$  alkoxy, or two or more of  $R_1, R_2, R_3, R_4, R_6, R_7, R_8, R_9, R_{10}, R_{12}, R_{13}, R_{14}$  and  $R_{19}$  can be linked by combination of the atoms of C, O, N, S, P and Si to form a 3 to 15 member ring(s), in the  $\alpha$ - and/or  $\beta$ - configuration;

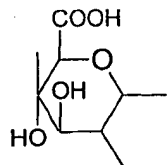
$R_5, R_6, R_{10}$ , and  $R_{11}$  are independently OH, SH, H, halogen, pharmaceutically acceptable ester, pharmaceutically acceptable thioester, pharmaceutically acceptable ether, pharmaceutically acceptable thioether, pharmaceutically acceptable inorganic esters, pharmaceutically acceptable monosaccharide, disaccharide or oligosaccharide, spirooxirane, spirothirane,  $-OSO_2R_{20}$ ,  $-OPOR_{20}R_{21}$ ,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkyne or  $OR_{23}$ ,  $-SO_2O-CH_2CHCH_2OCOR_{25}$

wherein,  $R_{23}$  is hydrogen or  $SO_2OM$ , wherein M is selected from H, Na, sulfatide;



$OCOR_{24}$  or

phosphatide  $OCOR_{24}$ , wherein  $R_{24}$  and  $R_{25}$ , which may be the same or different, are straight or branched  $(C_1-C_{20})$  alkyl,  $(C_1-C_{20})$  alkene,  $(C_1-C_{20})$  alkyne, sugar, polyethyleneglycol (PEG) or glucuronide



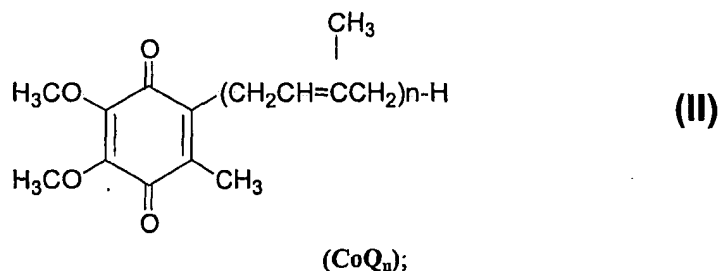
$R_5$  and  $R_6$  taken together are  $=O$ ;  
 $R_{10}$  and  $R_{11}$  taken together are  $=O$ ;

$R_{15}$  is (1) H, halogen,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkyne, or  $(C_1-C_{10})$  alkoxy when  $R_{16}$  is  $-C(O)OR_{22}$ , (2) H, halogen, OH,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene or  $(C_1-C_{10})$  alkyne, when  $R_{16}$  is halogen, OH,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene or  $(C_1-C_{10})$  alkyne, (3) H, halogen,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkenyl,  $(C_1-C_{10})$  alkynyl, formyl,  $(C_1-C_{10})$  alkanoyl or epoxy when  $R_{16}$  is OH, (4) OR, SR, SH, H, halogen, pharmaceutically acceptable ester, pharmaceutically acceptable thioester, pharmaceutically acceptable ether, pharmaceutically acceptable thioether, pharmaceutically acceptable inorganic esters, pharmaceutically acceptable monosaccharide, disaccharide or oligosaccharide, spirooxirane, spirothirane,  $-OSO_2R_{20}$  or  $-OPOR_{20}R_{21}$  when  $R_{16}$  is H, or  $R_{15}$  and  $R_{16}$  taken together are  $=O$ ;

$R_{17}$  and  $R_{18}$  are independently (1) H, -OH, halogen,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkyne or  $-(C_1-C_{10})$  alkoxy when  $R_6$  is H OR, halogen,  $(C_1-C_{10})$  alkyl or  $-C(O)OR_{22}$ , (2) H,  $(C_1-C_{10})$  alkyl<sub>n</sub> amino,  $(C_1-C_{10})$  alkene<sub>n</sub> amino,  $(C_1-C_{10})$  alkyne<sub>n</sub> amino,  $((C_1-C_{10})$  alkyl<sub>n</sub> amino- $(C_1-C_{10})$  alkyl,  $((C_1-C_{10})$  alkene<sub>n</sub> amino- $(C_1-C_{10})$  alkyl,  $((C_1-C_{10})$  alkyne<sub>n</sub> amino- $(C_1-C_{10})$  alkyl,  $((C_1-C_{10})$  alkyl<sub>n</sub> amino- $(C_1-C_{10})$  alkene,  $((C_1-C_{10})$  alkene<sub>n</sub> amino- $(C_1-C_{10})$  alkene,  $((C_1-C_{10})$  alkyne<sub>n</sub> amino- $(C_1-C_{10})$  alkene,  $((C_1-C_{10})$  alkyl<sub>n</sub> amino- $(C_1-C_{10})$  alkyne,  $((C_1-C_{10})$  alkene<sub>n</sub> amino- $(C_1-C_{10})$  alkyne,  $((C_1-C_{10})$  alkyne<sub>n</sub> amino- $(C_1-C_{10})$  alkyne,  $(C_1-C_{10})$  alkoxy, hydroxy -  $(C_1-C_{10})$  alkyl, hydroxy -  $(C_1-C_{10})$  alkene, hydroxy -  $(C_1-C_{10})$  alkyne,  $(C_1-C_{10})$  alkoxy -  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkoxy -  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkoxy -  $(C_1-C_{10})$  alkyne, (halogen)<sub>m</sub>  $(C_1-C_{10})$  alkyl, (halogen)<sub>m</sub>  $(C_1-C_{10})$  alkene, (halogen)<sub>m</sub>  $(C_1-C_{10})$  alkyne,  $(C_1-C_{10})$  alkanoyl, formyl,  $(C_1-C_{10})$  carbalkoxy or  $(C_1-C_{10})$  alkanoyloxy when  $R_{15}$  and  $R_{16}$  taken together are  $=O$ , (3)  $R_{17}$  and  $R_{18}$  taken together are  $=O$ ; (4)  $R_{17}$  and  $R_{18}$  taken together with the carbon to which they are attached form a 3-6 member ring containing 0 or 1 oxygen atom; or (5)  $R_{15}$  and  $R_{17}$  taken together with the carbons to which they are

attached form an epoxide ring;  $R_{20}$  and  $R_{21}$  are independently OH, pharmaceutically acceptable ester or pharmaceutically acceptable ether;  $R_{22}$  is H, (halogen)<sub>m</sub> (C<sub>1</sub>-C<sub>10</sub>) alkyl, (halogen)<sub>m</sub> (C<sub>1</sub>-C<sub>10</sub>) alkene, (halogen)<sub>m</sub> (C<sub>1</sub>-C<sub>10</sub>) alkyne, (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkene or (C<sub>1</sub>-C<sub>10</sub>) alkyne; n is 0, 1 or 2; and m is 1, 2 or 3,

- 5 or pharmaceutically or veterinarily acceptable salts thereof; and/or  
a ubiquinone of the chemical formula



- 10 wherein n=1 to 12, the agent being present in an amount effective for treating respiratory lung diseases and conditions, or for reducing levels of, or sensitivity to, adenosine or for increasing surfactant or ubiquinone levels in a subject's tissue (s), or pharmaceutically acceptable salts thereof.

- 15 The oligos and the anti-inflammatory steroids ("AIS") and/or ubiquinones (the second agent) are provided in the form of separate compositions and formulations together with a carrier or diluent, and optionally with other therapeutic agents and formulation additives. The first and second active agents are also provided as a single composition in combination with a carrier and other ingredients known in the art, and may be provided jointly or separately contained in a capsule or cartridge, and in the form of a kit. The drawings accompanying this patent form part of the disclosure of the invention, and further illustrate some aspects of the present invention as discussed below.

## 20 BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates the inhibition of HT-29 SF cells by DHEA.

Figures 2A and 2B illustrate the effects of different amounts of DHEA on cell cycle distribution in HT-29 SF cells.

- 25 Figures 3A and 3B illustrate the reversal of DHEA-induced growth inhibition in HT-29 cells treated with CON: Control; MVA: Mevalonic Acid; SQ: Squaline; CH: Cholesterol; DN: Deoxyribonucleosides; RN: Ribonucleosides.

Figures 4A, 4B, 4C and 4D illustrate the reversal of DHEA-induced G1 arrest in HT-29 SF cells for different durations of treatment with DHEA.

- 30 The invention will now be described in general in conceptual and experimental terms, with reference to specific examples. Other objects, advantages and features of the present invention will become apparent to those skilled in the art from the description that follows.

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

- 35 This invention arose from a desire by the inventor to improve on his own prior treatments and those of others for diseases of the respiratory and pulmonary tracts, as well as those that develop elsewhere in the mammalian body. While he previously provided a pioneering treatment for respiratory tract conditions employing oligonucleotide anti-sense to pre-selected targets, and a treatment for respiratory conditions employing dehydroepiandrosterones and ubiquinone, he reasoned further that their combination might produce unexpectedly superior results given their independent mechanisms. Moreover, he posited that the combination of low dose anti-sense oligonucleotide (oligo) therapy with steroids in general and/or ubiquinone therapy would afford the advantage of their independent lack of detrimental side effects when compared with other agents such as steroids alone, and many others that are generally fraught with detrimental side effects and by the need of administering high doses of therapeutic agents. The inventor's prior discovery that variously targeted anti-sense oligonucleotides (oligos) may be utilized therapeutically in the treatment of diseases or conditions which impair respiration, cause inflammation and/or allergy(ies) in the lung and elsewhere, constrict bronchial tissue, obstruct lung airways, deplete surfactant

secretion, and/or otherwise impede normal breathing, lead him to expand his work to their combination with steroids of broad classifications, whose association, either known or discovered by him, with respiratory and pulmonary diseases as well as heart, brain, kidney, skin and other conditions, e.g. ailments associated with hypoxia, infantile Respiratory Disorder Syndrome (RDS), Acute Respiratory Disorder Syndrome (ARDS), aging, cardiac disease, cardiovascular problems, asthma, respiratory distress syndrome, rhinitis, pain, cystic fibrosis (CF), pulmonary hypertension, pulmonary vasoconstriction, pulmonary fibrosis, emphysema, chronic obstructive pulmonary disease (COPD), allergic rhinitis, and cancers such as lung cancer, leukemias, lymphomas, carcinomas, and the like, including colon cancer, breast cancer, lung cancer, pancreatic cancer, hepatocellular carcinoma, kidney cancer, melanoma, etc., as well as all types of cancers which may metastasize or have metastasized to the lung(s), including breast, liver and prostate cancer, would clearly find an immediate therapeutic application. In general, many diseases and conditions are associated with or cause inflammation, constricted bronchial tissue or lung airways, depletion of surfactant secretion, or augmented respiratory tract allergy(ies), or otherwise impede normal breathing.

The present treatment employs two agents, the first agent being selective for specific targets associated with or mediating these symptoms, and when administered into the airways it is employed in doses up to 1000-fold lower than previously seen in the art. The other agent includes a steroid agent and/or a ubiquinone and provides a more generalized amelioration of the symptoms, also in the substantial absence of undesirable side effects. This treatment further improves on the inventor's prior separate oligonucleotide (oligo) treatment by selecting oligos of reduced adenosine content, or otherwise reducing their adenosine content to reduce the release of free adenosine (A) by breakdown of A-containing oligonucleotides (oligos), thereby avoiding activating adenosine receptors that aggravate bronchoconstriction, and respiratory tract inflammation and allergies, lung surfactant depletion, and the like. As further described below, this patent also provides for the substitution of other bases with a universal base(s) (U) when some characteristic is to be modified. This patent provides novel and improved compositions, formulations, kits and methods which afford greatly improved results when compared with previously known independent treatments for preventing and alleviating bronchoconstriction, allergy(ies), inflammation, breathing difficulties, surfactant depletion and blockage of airways, as well as for preventing and alleviating other conditions and diseases which, directly or indirectly, affect the lung tissue. In different embodiments, one or more nucleic acids of the invention may be formulated for their administration alone or in combination with the steroid agents and/or ubiquinones, surfactant(s), a carrier, and/or other therapeutic agents and formulation agents known in the art. Similarly, the anti-inflammatory steroids and the ubiquinones may be formulated separately for separate administration, or with various formulation components, other therapeutic agents, and the like. By means of example, the steroids and ubiquinone may be administered once or twice daily whereas the oligo may only need be administered once weekly or biweekly.

The single or multiple active agent compositions of this invention are provided in a variety of systemic and topical formulations suitable for the delivery of anti-sense oligonucleotides (oligos) and anti-inflammatory steroids and/or ubiquinones by different routes as a fast means of starting treatment to address asthma and other pulmonary and respiratory tract diseases that may have a rapid onset, where a very low drug dosage is desirable. On the other hand, the oligos have long half-lives and may be administered as preventative of acute episodes, to significantly reduce emergency visits to a doctor or hospital, and as prophylactic maintenance treatment due to the high tolerability of the active agents for prolonged periods of time. In one embodiment, the present treatment provides a once-a-week oligo therapy, accompanied by daily administration of ubiquinone and/or a steroid incorporated into a subject's daily routine. This regime may be effectively administered preventatively, prophylactically and therapeutically, in conjunction with other therapies, or by itself for conditions without known therapies or as a substitute for therapies that have significant negative side effects is also of immediate clinical application. The present treatment also finds an application in the treatment of malignancies, given that steroids and ubiquinones are known for their carcinogenic activities as well as beneficial respiratory effects.

In these cases, the oligo are targeted to cancer-associated nucleic acids and their products. General examples of oligo(s) of the invention are those targeted to a receptor(s) and it (they) are typically present in the composition in an amount effective to reduce that receptor(s) mediated effect(s), and for reducing airway obstruction, lung inflammation and allergy(ies), and surfactant depletion, among others. In one embodiment the receptor is preferably an adenosine receptor such as the adenosine A<sub>1</sub>, A<sub>2b</sub>, or A<sub>3</sub> receptors, and in some instances even adenosine A<sub>2a</sub> receptors. The oligo of the invention may be applied to the preparation of a medicament for reducing bronchoconstriction, impeded respiration, lung inflammation and allergy(ies), depletion of surfactant or

ubiquinone, and for treating respiratory and pulmonary conditions in general, and specific ones such as asthma, ARDS, pulmonary fibrosis, cystic fibrosis, allergic rhinitis, COPD, etc. Many of the conditions targeted by the present treatment afflict a large segment of the population, and either remain unaddressed in terms of therapy or the existing treatments, although heavily advertised, are only mildly effective in small numbers of the afflicted population.

ARDS' most common symptoms are labored, rapid breathing, nasal flaring, cyanosis blue skin, lips and nails caused by lack of oxygen to the tissues, breathing difficulty, anxiety, stress, tension, joint stiffness, pain and temporarily absent breathing. In the following paragraphs, the specific conditions will be described, and the existing treatments, if any, discussed. ARDS is currently diagnosed by mere symptomatic signs, e. g. chest auscultation with a stethoscope that may reveal abnormal symptomatic breath sounds, and confirmed with chest X-rays and the measurement of arterial blood gas. ARDS, in some instances, appears to be associated with other diseases, such as acute myelogenous leukemia, acute tumor lysis syndrome (ATLS) developed after treatment with, e.g. cytosine arabinoside, etc. In general, however, ARDS is associated with traumatic injury, severe blood infections such as sepsis or other systemic illness, high-dose radiation therapy and chemotherapy, and inflammatory responses which lead to multiple organ failure and in many cases death. In premature babies ("premies"), the lungs are not quite developed and, therefore, the fetus is in an anoxic state during development. Moreover, lung surfactant, a material critical for normal respiration, is generally not yet present in sufficient amounts at this early stage of life; however, premies often hyper-express the adenosine A<sub>1</sub> receptor and/or underexpress the adenosine A<sub>2a</sub> receptor and are, therefore, susceptible to respiratory problems including bronchoconstriction, lung inflammation and ARDS, among others. When Respiratory Distress Syndrome (RDS) occurs in premies, it is an extremely serious problem. Preterm infants exhibiting RDS are currently treated by ventilation and administration of oxygen and surfactant preparations. When premies survive RDS, they frequently develop bronchopulmonary dysplasia (BPD), also called chronic lung disease of early infancy, which is often fatal.

Rhinitis may be seasonal or perennial, allergic or non-allergic. Non-allergic rhinitis may be induced by infections, such as viruses, or associated with nasal polyps, as occurs in patients with aspirin idiosyncrasy. Medical conditions such as pregnancy or hypothyroidism and exposure to occupational factors or medications may cause rhinitis. The so-called NARES syndrome is a non-allergic type of rhinitis associated with eosinophils in the nasal secretions, which typically occurs in middle-age and is accompanied by some loss of sense of smell. When cholinergic pathways are stimulated they produce typical secretions that are identified by their glandular constituents so as to implicate neurologic stimulation. Other secretions typical of increased vascular permeability are found in allergic reactions as well as upper respiratory infections, and the degranulation of mast cells releases preformed mediators that interact with various cells, blood vessels, and mucous glands, to produce the typical rhinitis symptoms. Most early- and late-phase reactions occur in the nose after allergen exposure. The late-phase reaction is seen in chronic allergic rhinitis, with hypersecretion and congestion as the most prominent symptoms. When priming occurs, it exhibits a lowered threshold to stimulus after repeated allergen exposure that, in turn, causes a hypersensitivity reaction to one or more allergens. Sufferers may also become hyper-reactive to non-specific triggers such as cold air or strong odors. Saline sprays are generally used to relieve mucosal irritation or dryness associated with various nasal conditions, minimize mucosal atrophy, and dislodge encrusted or thickened mucus and are used immediately before intranasal corticosteroid dosing to prevent drug-induced local irritation. Anti-histamines such as terfenadine and astemizole, two non-sedating anti-histamines, are also employed to treat this condition, but have been associated with a ventricular arrhythmia known as Torsades de Points, usually in interaction with other medications such as ketoconazole and erythromycin, or secondary to an underlying cardiac problem. Loratadine, another non-sedating anti-histamine, and cetirizine have not been associated with an adverse impact on the QT interval, or with serious adverse cardiovascular events. Cetirizine, however, produces extreme drowsiness and has not been widely prescribed. Non-sedating anti-histamines, e.g. Claritin have not been tested for asthma or other more specific conditions. Terfenadine, loratadine and astemizole, on the other hand, exhibit extremely modest bronchodilating effects, reduction of bronchial hyper-reactivity to histamine, and protection against exercise- and antigen-induced bronchospasm. Some of these benefits, however, require higher-than-currently-recommended doses. The sedating-type anti-histamines help induce night sleep, but they cause sleepiness and compromise performance if taken during the day.

When employed, anti-histamines are typically combined with a decongestant to help relieve nasal congestion. Sympathomimetic medications are used as vasoconstrictors and decongestants. The three commonly prescribed systemic decongestants, pseudoephedrine, phenylpropanolamine and phenylephrine cause hypertension,

palpitations, tachycardia, restlessness, insomnia and headache. The interaction of phenylpropanolamine with caffeine, in doses of two to three cups of coffee, may significantly raise blood pressure. In addition, medications such as pseudoephedrine may cause hyperactivity in children. Topical decongestants, nevertheless, are only indicated for a limited period of time, as they are associated with a rebound nasal dilatation with overuse. Anti-cholinergic agents are given to patients with significant rhinorrhea or for specific conditions such as "gustatory rhinitis", usually caused by ingestion of spicy foods, and may have some beneficial effects on the common cold. Cromolyn used prophylactically as a nasal spray, however, produces sneezing, transient headache, and even nasal burning. Topical corticosteroids, such as Vancenase, are somewhat effective in the treatment of rhinitis, especially for symptoms of congestion, sneezing, and runny nose. Corticosteroid nose sprays, however, sometimes, cause irritation, stinging, burning and sneezing, and sometimes local bleeding and septal perforation. The side effects of topical steroids, however, limit their usefulness except for temporary therapy in patients with severe symptoms. These agents are sometimes used for shrinking nasal polyps when local therapy fails. Immunotherapy is expensive and inconvenient, and used mostly in in-patients who experience side effects from other medications. The so-called blocking antibodies, and agents that alter cellular histamine release, in addition, decrease IgE, which is useful in IgE-mediated diseases, e.g., hypersensitivity in atopic patients with recurrent middle ear infections. For allergic rhinitis sufferers, however, a runny nose is more than a nuisance. The disorder often results in impaired quality of life and sets the stage for more serious ailments, including psychological problems. Presently, rhinitis is mostly treated with propranolol, verapamil, and adenosine, all of which have Food and Drug Administration-approved labeling for acute termination of Supraventricular Tachycardia (SVT).

There is very little currently available to alleviate symptoms of COPD, prevent exacerbations, preserve optimal lung function, and improve daily living activities and quality of life. Anti-cholinergic drugs achieve short-term bronchodilation, but no improved long-term prognosis even with inhaled products. Most COPD patients have at least some airways obstruction, and "the lung health study" found spirometric signs of early COPD in men and women smokers. Smoking cessation produced a slowing of the decline in the functional effective volume of the lungs. While ipratropium bromide was found to have no significant effect on the decline in the functional effective volume of the patient's lungs. Ipratropium bromide, however, produced serious adverse effects, such as cardiac symptoms, hypertension, skin rashes, and urinary retention. Short and long acting inhaled  $\beta_2$  adrenergic agonists achieve short-term bronchodilation and provide some symptomatic relief in COPD patients, but show no meaningful maintenance effect on its progression. Short acting  $\beta_2$  adrenergic agonists increase exercise capacity and produce some degree of bronchodilation, and even increase lung function in some severe COPD cases. The maximum effectiveness of the newer long acting inhaled  $\beta_2$  adrenergic agonists was found to be comparable to that of short acting  $\beta_2$  adrenergic agonists. Salmeterol was found to produce modest or no change in lung function. In asthmatics, moreover,  $\beta_2$  adrenergic agonists have been linked to an increased risk of death, worsened control of asthma, and deterioration in lung function.

Continuous treatment of asthmatic and COPD patients with the bronchodilators ipratropium bromide or fenoterol resulted in a decline in lung function, therefore indicating that they are not suitable for maintenance treatment. The most common immediate adverse effect of  $\beta_2$  adrenergic agonists, however, is tremors, which at high doses may cause a fall in plasma potassium, dysrhythmias, and reduced arterial oxygen tension. The combination of a  $\beta_2$  adrenergic agonist with an anti-cholinergic drug provides little additional bronchodilation compared with either drug alone. Theophyllines have a small bronchodilatory effect in COPD patients but common adverse effects, such as nausea, diarrhea, headache, irritability, seizures, and cardiac arrhythmias, that occur at highly variable blood concentrations and, in many people, within the therapeutic range. In addition, they have a small therapeutic range given that blood concentrations of 15-20 mg/l are required for optimal effects. The theophylline dose must be adjusted individually based on smoking habits, infection, and other treatments, which is cumbersome. No inflammatory response to theophyllines, however, has been reported in COPD. Oral corticosteroids show some improvement in baseline functional effective volume in stable COPD patients whereas systemic corticosteroids have been found to produce some degree of osteoporosis and overt diabetes. The longer term use of oral corticosteroids may be useful in COPD, but its usefulness must be weighed against their substantial adverse effects. Inhaled corticosteroids have been found to have no significant short-term effect in airway hyper-responsiveness to histamine, but a small long-term effect on lung function, e.g., in pre-bronchodilator functional effective volume. The treatment of COPD patients with fluticasone showed a significant reduction in moderate and severe exacerbations, and a small but significant improvement in lung function and six minute walking distance. Oral prednisolone, inhaled

beclomethasone or their combination had no effects in COPD patients, but lung function improved oral corticosteroids. Mucolytics have a modest effect on frequency and duration of exacerbations but an adverse effect on lung function. No mucolytics, however, have a significant effect in people with severe COPD. N-acetylcysteine, moreover, produced gastrointestinal side effects. Long-term oxygen therapy administered to hypoxaemic COPD and congestive cardiac failure patients, had little effect on death in men. In women, however, oxygen decreased the rates of death.

Although the progress and symptoms of pulmonary fibrosis and other ILDs may vary from person to person, they have one common link: they affect parts of the lung. The inflammation of the walls of the bronchioles (small airways), it is called bronchiolitis, and of the walls and air spaces of the alveoli (air sacs), it is called alveolitis. When the inflammation involves the small blood vessels (capillaries) of the lungs, it is called vasculitis. The inflammation may heal, or it may lead to permanent scarring of the lung tissue (pulmonary fibrosis). This latter results in permanent loss of the tissues ability to breathe and carry oxygen, and the amount of scarring determines the level of disability a person experiences due to destruction of the air sacs and lung tissue between and surrounding the air sacs and the lung capillaries. When this happens, oxygen is generally administered to help improve breathing. Pulmonary fibrosis is generally caused by occupational and environmental exposure to irritants such as asbestos, silica and metal dusts, bacteria and animal dusts, gases and fumes, asbestosis and silicosis, infections that produce lung scarring, e.g., tuberculosis, connective or collagen tissue diseases such as Rheumatoid Arthritis, Systemic Sclerosis and Systemic Lupus Erythematosus, Idiopathic Pulmonary Fibrosis, Pulmonary Fibrosis of genetic/familial origin, and certain medicines. Many of the diseases are often named after the occupations with which they are associated, such as Grain handler's lung, Mushroom worker's lung, Bagassosis, Detergent worker's lung, Maple bark stripper's lung, Malt worker's lung, Paprika splitter's lung, and Bird breeder's lung.

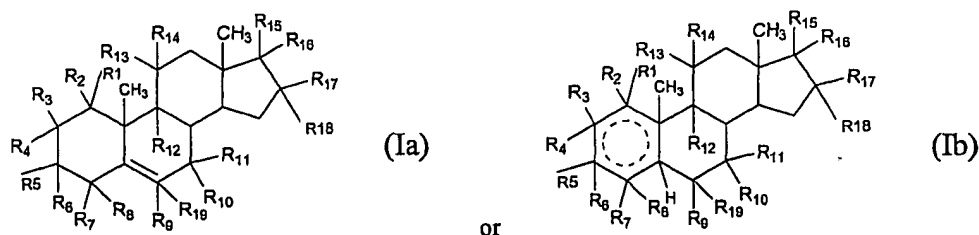
"Idiopathic" (of unknown origin) pulmonary fibrosis (IPF) is the label applied when all other causes of interstitial lung disease have been ruled out, and is said to be caused by viral illness and allergic or environmental exposure (including tobacco smoke). Bacteria and other microorganisms are not thought to be a cause of IPF. There is also a familial form of the disease, known as familial idiopathic pulmonary fibrosis whose main symptom is shortness of breath. Since many lung diseases show this symptom, making a correct diagnosis is often difficult. The shortness of breath may first appear during exercise and the condition may progress then to the point where any exertion is impossible. Eventually resulting in shortness of breath even at rest. Other symptoms may include a dry cough (without sputum), and clubbing of the fingertips. Glucocorticosteroids are usually administered to treat inflammation with inconclusive results. Other drugs are added when it is clear that the steroids are ineffective. Glucocorticosteroids are also used in combination with, for example, oxygen therapy in severe cases. Infection is prevented by administration of influenza and pneumococcal pneumonia vaccines. Lung biopsies are employed to assess the unpredictable response of patients to glucocorticosteroids or other immune system suppressants. Lung transplants are an ultimate option in severe cases of pulmonary fibrosis and other lung diseases. Pulmonary fibrosis may be caused by other specific diseases, such as sarcoidosis, a disease characterized by the formation of granulomas or areas of inflammatory cells, that may attack any organ of the body, most frequently the lungs, and shows enlarged lymph glands in the center of both lungs or lung tissue thickening. For many patients, sarcoidosis is a minor problem. Its symptoms including dry cough, shortness of breath, mild chest pain, fatigue, and weakness, and weight loss appears infrequently and stops even without medication. For others, it is a serious, disabling disease. Although almost everybody may develop the disease, it affects African-Americans more than members of any other race, most commonly young adults 20 to 40. Histiocytosis X, also associated with pulmonary fibrosis, seems to begin in the bronchioles or small airways of the lungs and their associated arteries and veins, and is generally followed by destruction of the bronchioles and narrowing and damaging of small blood vessels. Symptoms of this disease include a dry cough (without sputum), breathlessness upon exertion, and/or chest pain. In most cases the disease is chronic with loss of lung function, and glucocorticosteroid therapy is ineffective. Many histiocytosis X sufferers are current or former cigarette smokers mining workers, those exposed to asbestos or metal dusts or fibers, and agricultural workers exposed to particulate organic substances, such as moldy hay (Farmer's Lung). Asbestosis and silicosis are two occupational lung diseases whose causes are known. Asbestosis is caused by small needle-like particles of asbestos inhaled into the lungs that cause lung scarring or pulmonary fibrosis that may lead to lung cancer. Silicosis is a dust disease that comes from breathing in free crystalline silica dust, and is produced by all types of mining in which the ore, e. g. gold, lead, zinc, copper, iron, anthracite (hard) coal, and some bituminous (soft) coal, are extracted from quartz rock. Workers in foundries, sandstone grinding, tunneling, sandblasting,

concrete breaking, granite carving, and china manufacturing also inhaled tiny specks of silica that are carried down to the lung alveoli, where they lead to pulmonary fibrosis. There is no good therapy for this disease, but glucocorticosteroids alone, or combined drug therapy, and the hope of lung transplant are three treatments currently being tested. This patent provides the first effective therapy for these and other respiratory and lung ailments.

In the present context, the terms “adenosine, surfactant and ubiquinone depletion” are intended to encompass levels that are lowered or depleted in the subject as compared to previous levels in that subject, and levels, as well as levels in that subject but, because of some other reason, a therapeutic benefit would be achieved in the patient by modification of the levels of these agents as compared to previous levels.

The present invention, thus, provides a pharmaceutical or veterinary composition, comprising a pharmaceutically or veterinarily acceptable carrier or diluent, a first active agent comprising an anti-sense oligonucleotide(s) (oligo(s)), and a second active agent comprising an anti-inflammatory steroid and/or a ubiquinone, in amounts effective for alleviating a variety of airway or lung diseases, and other diseases such as cancers or their metastasis, among others. This invention provides the targeted administration of one or more oligo(s) in combination with a second active agent that has a more generalized effect as an anti-inflammatory, and alleviates bronchoconstriction, surfactant or ubiquinone depletion, and respiratory airway allergies. The oligos may be directed to one or more of a number of targets, and are delivered by any route, preferably through the airways to attain a fast and localized delivery through the mucosal tissue of the lungs to permit their hybridization to a desired target polynucleotide to prevent gene transcription and/or translation, thereby reducing, hampering or completely stopping gene expression. This may be attained by means of a solid powdered or liquid solution, suspension or emulsion, such as an aerosol, for administration into the respiratory airways, or direct instillation into the lung(s). While both active agents may be administered via the respiration, it is also possible to administer one by another route, e.g. steroids. The oligos employed in the composition are suitable for altering effects mediated by a variety of target polynucleic acids, such as regulatory nucleic acid sequences, genes and mRNAs, that are associated with diseases and conditions affecting the pulmonary and respiratory tracts, among others, and their associated effects, e.g. bronchoconstriction, respiratory tract inflammation, immune mediated reactions, lung surfactant deficiency(ies), respiratory allergy(ies) and other airway problems, which may be caused by different conditions, including pulmonary vasoconstriction, inflammation, respiratory allergies, asthma, impeded respiration, respiratory distress syndrome (RDS), pain, cystic fibrosis (CF), allergic rhinitis, pulmonary hypertension and fibrosis, sepsis, dyspnea, acute respiratory distress syndrome (ARDS), as well as its variations in pregnant mothers and new-borns (RDS), pulmonary fibrosis, emphysema, chronic obstructive pulmonary disease (COPD), bronchitis, and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. lung cancer, colon cancer, breast cancer, pancreatic cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastases, etc., as well as all cancers which may metastasize or have metastasized to the lung(s), including breast and prostate cancer. The present agents are also suitable for administration before, during and after other treatments, including radiation, chemotherapy, antibody therapy, phototherapy, and cancer and other surgeries.

The second active agent is selected from an anti-inflammatory steroid such as an adrenal androgen of the chemical formula



wherein R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub>, R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub> and R<sub>19</sub> are independently H, OR, halogen, (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkene, (C<sub>1</sub>-C<sub>10</sub>) alkyne, (C<sub>1</sub>-C<sub>10</sub>) alkoxy, or two or more of R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub>, R<sub>9</sub>, R<sub>10</sub>, R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub> and R<sub>19</sub> can be linked by combination of the atoms of C, O, N, S, P and Si to form a 3 to 15 member ring(s), in the  $\alpha$ - and/or  $\beta$ - configuration;

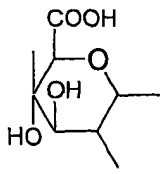
R<sub>5</sub>, R<sub>6</sub>, R<sub>10</sub>, and R<sub>11</sub> are independently OH, SH, H, halogen, pharmaceutically acceptable ester, pharmaceutically acceptable thioester, pharmaceutically acceptable ether, pharmaceutically acceptable thioether, pharmaceutically acceptable inorganic esters, pharmaceutically acceptable monosaccharide, disaccharide or oligosaccharide, spirooxirane, spirothirane, -OSO<sub>2</sub>R<sub>20</sub>, -OPOR<sub>20</sub>R<sub>21</sub>, (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkene, (C<sub>1</sub>-C<sub>10</sub>) alkyne or OR<sub>23</sub>,  

$$\begin{array}{c} \text{-SO}_2\text{O-CH}_2\text{CHCH}_2\text{OCOR}_{25} \\ | \\ \text{OCOR}_{24} \end{array}$$

- 5 wherein, R<sub>23</sub> is hydrogen or SO<sub>2</sub>OM, wherein M is selected from H, Na, sulfate;  

$$\begin{array}{c} \text{-PO}_2\text{O-CH}_2\text{CHCH}_2\text{OCOR}_{25} \\ | \\ \text{OCOR}_{24} \end{array}$$

phosphatide , wherein R<sub>24</sub> and R<sub>25</sub>, which may be the same or different, are straight or branched (C<sub>1</sub>-C<sub>20</sub>) alkyl, (C<sub>1</sub>-C<sub>20</sub>) alkene, (C<sub>1</sub>-C<sub>20</sub>) alkyne, sugar, polyethyleneglycol (PEG) or glucuronide



R<sub>5</sub> and R<sub>6</sub> taken together are =O;

- 10 R<sub>10</sub> and R<sub>11</sub> taken together are =O;

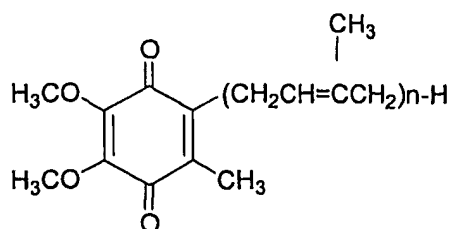
R<sub>15</sub> is (1) H, halogen, (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkene, (C<sub>1</sub>-C<sub>10</sub>) alkyne, or (C<sub>1</sub>-C<sub>10</sub>) alkoxy when R<sub>16</sub> is -C(O)OR<sub>22</sub>, (2) H, halogen, OH, (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkene or (C<sub>1</sub>-C<sub>10</sub>) alkyne, when R<sub>16</sub> is halogen, OH, (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkene or (C<sub>1</sub>-C<sub>10</sub>) alkyne, (3) H, halogen, (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkenyl, (C<sub>1</sub>-C<sub>10</sub>) alkynyl, formyl, (C<sub>1</sub>-C<sub>10</sub>) alkanoyl or epoxy when R<sub>16</sub> is OH, (4) OR, SR, SH, H, halogen, pharmaceutically acceptable ester, pharmaceutically acceptable thioester, pharmaceutically acceptable ether, pharmaceutically acceptable thioether, pharmaceutically acceptable inorganic esters, pharmaceutically acceptable monosaccharide, disaccharide or oligosaccharide, spirooxirane, spirothirane, -OSO<sub>2</sub>R<sub>20</sub> or -OPOR<sub>20</sub>R<sub>21</sub> when R<sub>16</sub> is H, or R<sub>15</sub> and R<sub>16</sub> taken together are =O;

20

R<sub>17</sub> and R<sub>18</sub> are independently (1) H, -OH, halogen, (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkene, (C<sub>1</sub>-C<sub>10</sub>) alkyne or -(C<sub>1</sub>-C<sub>10</sub>) alkoxy when R<sub>6</sub> is H OR, halogen, (C<sub>1</sub>-C<sub>10</sub>) alkyl or -C(O)OR<sub>22</sub>, (2) H, (C<sub>1</sub>-C<sub>10</sub>) alkyl)<sub>n</sub> amino, (C<sub>1</sub>-C<sub>10</sub>) alkene)<sub>n</sub> amino, (C<sub>1</sub>-C<sub>10</sub>) alkyne)<sub>n</sub> amino, ((C<sub>1</sub>-C<sub>10</sub>) alkyl)<sub>n</sub> amino-(C<sub>1</sub>-C<sub>10</sub>) alkyl, ((C<sub>1</sub>-C<sub>10</sub>) alkene)<sub>n</sub> amino-(C<sub>1</sub>-C<sub>10</sub>) alkyl, ((C<sub>1</sub>-C<sub>10</sub>) alkyne)<sub>n</sub> amino-(C<sub>1</sub>-C<sub>10</sub>) alkyl, ((C<sub>1</sub>-C<sub>10</sub>) alkyl)<sub>n</sub> amino-(C<sub>1</sub>-C<sub>10</sub>) alkene, ((C<sub>1</sub>-C<sub>10</sub>) alkene)<sub>n</sub> amino-(C<sub>1</sub>-C<sub>10</sub>) alkene, ((C<sub>1</sub>-C<sub>10</sub>) alkyne)<sub>n</sub> amino-(C<sub>1</sub>-C<sub>10</sub>) alkene, ((C<sub>1</sub>-C<sub>10</sub>) alkyl)<sub>n</sub> amino-(C<sub>1</sub>-C<sub>10</sub>) alkyne, ((C<sub>1</sub>-C<sub>10</sub>) alkene)<sub>n</sub> amino-(C<sub>1</sub>-C<sub>10</sub>) alkyne, ((C<sub>1</sub>-C<sub>10</sub>) alkyne)<sub>n</sub> amino-(C<sub>1</sub>-C<sub>10</sub>) alkyne, (C<sub>1</sub>-C<sub>10</sub>) alkoxy, hydroxy - (C<sub>1</sub>-C<sub>10</sub>) alkyl, hydroxy - (C<sub>1</sub>-C<sub>10</sub>) alkene, hydroxy - (C<sub>1</sub>-C<sub>10</sub>) alkyne, (C<sub>1</sub>-C<sub>10</sub>) alkoxy - (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkoxy - (C<sub>1</sub>-C<sub>10</sub>) alkene, (C<sub>1</sub>-C<sub>10</sub>) alkoxy - (C<sub>1</sub>-C<sub>10</sub>) alkyne, (halogen)<sub>m</sub> (C<sub>1</sub>-C<sub>10</sub>) alkyl, (halogen)<sub>m</sub> (C<sub>1</sub>-C<sub>10</sub>) alkene, (halogen)<sub>m</sub> (C<sub>1</sub>-C<sub>10</sub>) alkyne, (C<sub>1</sub>-C<sub>10</sub>) alkanoyl, formyl, (C<sub>1</sub>-C<sub>10</sub>) carbalkoxy or (C<sub>1</sub>-C<sub>10</sub>) alkanoyloxy when R<sub>15</sub> and R<sub>16</sub> taken together are =O, (3) R<sub>17</sub> and R<sub>18</sub> taken together are =O; (4) R<sub>17</sub> and R<sub>18</sub> taken together with the carbon to which they are attached form a 3-6 member ring containing 0 or 1 oxygen atom; or (5) R<sub>15</sub> and R<sub>17</sub> taken together with the carbons to which they are attached form an epoxide ring; R<sub>20</sub> and R<sub>21</sub> are independently OH, pharmaceutically acceptable ester or pharmaceutically acceptable ether; R<sub>22</sub> is H, (halogen)<sub>m</sub> (C<sub>1</sub>-C<sub>10</sub>) alkyl, (halogen)<sub>m</sub> (C<sub>1</sub>-C<sub>10</sub>) alkene, (halogen)<sub>m</sub> (C<sub>1</sub>-C<sub>10</sub>) alkyne, (C<sub>1</sub>-C<sub>10</sub>) alkyl, (C<sub>1</sub>-C<sub>10</sub>) alkene or (C<sub>1</sub>-C<sub>10</sub>) alkyne; n is 0, 1 or 2; and m is 1, 2 or 3; or pharmaceutically or veterinarily acceptable salts thereof; and/or

35

a ubiquinone of the chemical formula



(III)

(CoQ<sub>n</sub>),



wherein n is 1 to 12, the agent being present in an amount effective for treating respiratory lung diseases and conditions, or for reducing levels of, or sensitivity to, adenosine in a subject's tissue (s); and/or pharmaceutically acceptable salts of either of them.

One group of preferred steroids having a general formula (Ib) are 21-acetoxypregnenolone ((3 $\beta$ )-21-(acetyloxy)-3-hydroxypregn-5-en-20-one; Herloff and Inhoffen, US Patent No. 2,409,043); alclometasone ((7 $\alpha$ , 11 $\beta$ , 16 $\alpha$ )-7-Chloro-11, 17, 21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione; Green et al., US Patent No. 4,076,708, and Green and Shue, US Patent No. 4,124,707), or its 17,21-dipropionate form (C<sub>28</sub>H<sub>37</sub>ClO<sub>7</sub>); algestone ((16 $\alpha$ )-16,17-dihydroxypregn-4-ene-3,20-dione; Colton, US Patent No. 2,727,909, Hydorn et al., US Patent No. 3,165,541, and Diassi, US Patent No. 3,027,384), its cyclic acetal with acetone form (C<sub>24</sub>H<sub>34</sub>O<sub>4</sub>), or its 16 $\alpha$ -methyl ether form (C<sub>22</sub>H<sub>32</sub>O<sub>4</sub>); amcinonide ((11 $\beta$ , 16 $\alpha$ )-21-(acetyloxy)-16,17-[cyclopentylidenebis(oxy)]-9-fluoro-11-hydroxypregna-1,4-di-ene-3,20-dione; Shultz et al., German Patent No. 2,437,847); beclomethasone ((11 $\beta$ ,16 $\beta$ )-9-chloro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione; British Patent No. 912,378, British Patent No. 901,093, Elks et al., Belgium Patent No. 649,170, and US Patent No. 3,312,590), its dipropionate form (C<sub>28</sub>H<sub>37</sub>ClO<sub>7</sub>), or its monopropionate form; betamethasone ((11 $\beta$ , 16 $\beta$ )-9-fluoro-11, 17, 21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione; US Patent No. 3,053,865, and Amiard et al., US Patent No. 3,104,246), its 21-acetate form (C<sub>24</sub>H<sub>31</sub>FO<sub>6</sub>), its 21-adamantoate form (C<sub>33</sub>H<sub>43</sub>FO<sub>6</sub>; Philips and English, German Patent No. 2,232,827), its 17-benzoate form (C<sub>29</sub>H<sub>33</sub>FO<sub>6</sub>), its 17, 21-dipropionate form (C<sub>28</sub>H<sub>37</sub>FO<sub>7</sub>), its 17-valerate form (C<sub>27</sub>H<sub>37</sub>FO<sub>6</sub>; Dutch Patent Application No. 6,406,615), or its 21-phosphate disodium salt form (C<sub>22</sub>H<sub>28</sub>FNa<sub>2</sub>O<sub>8</sub>P); budesonide ((11 $\beta$ , 16 $\alpha$ )-16,17-[butylidenebis(oxy)]-11, 21-dihydropregna-1,4-diene-3,20-dione; Brattsand et al., German Patent No. 2,323,215, and US Patent No. 3,929,768); chloroprednisone ((6 $\alpha$ )-chloro-17,21-dihydroxypregna-1,4-diene-3,11,20-trione; Batres et al., German Patent No. 1,079,042, and Ringold and Rosenkrantz, US Patent No. 2,957,895), or its 21-acetate form (C<sub>23</sub>H<sub>27</sub>ClO<sub>6</sub>); ciclesonide (Taylor et al., Am J Respir Crit Care Med (1999) 160(1), 237-43); clobetasol ((11 $\beta$ ,16 $\beta$ )-21-chloro-9-fluoro-11,17-dihydroxy-16-methylpregna-1,4-diene-3,20-dione; Elks et al., German Patent No. 1,902,340, and US Patent No. 3,721,687), or its 17-propionate form (C<sub>25</sub>H<sub>32</sub>ClFO<sub>5</sub>); clobetasone ((16 $\beta$ )-21-chloro-9-fluoro-17-hydroxy-16-methylpregna-1,4-diene-3,11,20-trione; Elks et al., German Patent No. 1,902,340, and US Patent No. 3,721,687), or its 17-butyrate form (C<sub>26</sub>H<sub>32</sub>ClFO<sub>5</sub>); clo cortolone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-9-chloro-6-fluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione; Dutch Patent Application No. 6,412,708, Kasper and Philipsson, German Patent No. 2,011,559, and US Patent No. 3,729,495), its 21-acetate form (C<sub>24</sub>H<sub>30</sub>ClFO<sub>5</sub>), or its 21-pivalate form (C<sub>27</sub>H<sub>36</sub>ClFO<sub>5</sub>); cloprednol ((11 $\beta$ )-6-chloro-11,17,21-trihydroxypregna-1,4,6-triene-3,20-dione; France Patent No. 1,271,981, and US Patent No.3,232,965); coroxon (phosphoric acid 3-chloro-4-methyl-2-oxo-2H-1-benzopyran-7-yl diethyl ester; Fusco et al., US Patent No. 2,951,851); cortisone (17,21-dihydroxypregn-4-ene-3,11,20-trione; Reichstein, US Patent No. 2,403,683, and Gallagher, US Patent No. 2,447,325), its 21-acetate form (C<sub>23</sub>H<sub>30</sub>O<sub>6</sub>), or its 21-cyclopentanepropionate form (C<sub>29</sub>H<sub>40</sub>O<sub>6</sub>), examples of brand name for cortisone include Cortone Acetate, Adreson, Altesona, Cortelan, Cortistab, Cortisyl, Cortogen, Cortone, and Scheroson; cortivazol ((11 $\beta$ ,16 $\alpha$ )-21-(acetyloxy)-11,17-dihydroxy-6,16-dimethyl-2'-phenyl-2'-H-pregna-2,4,6-trieno[3,2-c]pyrazol-20-one; Tishler et al., US Patent No. 3,067,194, and US Patent No. 3,300,483); deflazacort ((11 $\beta$ ,16 $\beta$ )-21-(acetyloxy)-11-hydroxy-2'-methyl-5'-H-pregna-1,4-dieno[17,16-d]oxazole-3,20-dione; Nathansohn and Winters, Belgium Patent No. 679,820, British Patent No. 1,077,393, and US Patent No. 3,436,389); desonide ((11 $\beta$ ,16 $\alpha$ )-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione; Bernstein and Allen, US Patent No. 2,990,401, Lee et al., US Patent No. 3,536,586, and Diassi and Principe, US Patent No. 3,549,498); desoximetasone ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11, 21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione; Joly et al., France Patent No. 1,296,544, US Patent No. 3,099,654, Belgium Patent No. 614,196, and Kieslich et al., US Patent No. 3,232,839); dexamethasone ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione; Muller et al., US Patent No. 3,007,923, Arth et al., German Patent No. 1,113,690, and British Patent No. 869,511), its 21-acetate form (C<sub>24</sub>H<sub>31</sub>FO<sub>6</sub>), its 21-(3,3-dimethylbutyrate) form (C<sub>28</sub>H<sub>39</sub>FO<sub>6</sub>; Chemerda et al., US Patent No. 2,939,873), its 21-diethylaminoacetate form (C<sub>28</sub>H<sub>41</sub>FNO<sub>6</sub>), its 21-isonicotinate form (C<sub>28</sub>H<sub>41</sub>FNO<sub>6</sub>), its 17,21-dipropionate form (C<sub>28</sub>H<sub>37</sub>FNO<sub>6</sub>), or its 21-palmitate form (C<sub>38</sub>H<sub>59</sub>FO<sub>6</sub>), examples of brand name for dexamethasone include Decadron-oral, Dexameth, Dexone, Hexadrol-oral, Dexamethasone Intensol, Dexone 0.5, Dexone 0.75, Dexone 1.5, and Dexone 4; diflorasone ((6 $\alpha$ ,11 $\beta$ ,16 $\beta$ )-6,9-difluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione; British Patent No. 881,334, British Patent No. 898,293, Lincoln et al., US Patent No. 3,557,158, and British Patent No. 912,015), or its diacetate form (C<sub>26</sub>H<sub>32</sub>F<sub>2</sub>O<sub>7</sub>; Ayer et al., German Patent No. 2,308,731, and

US Patent No. 3,980,778); diflucortolone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6,9-difluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione; Belgium Patent No. 639,708, and Kieslich et al., US Patent No.3,426,128), or its 21-valerate form (C<sub>27</sub>H<sub>36</sub>F<sub>2</sub>O<sub>5</sub>); difluprednate ((6 $\alpha$ ,11 $\beta$ )-21-(acetyloxy)-6,9-difluoro-11-hydroxy-17-(1-oxobutoxy)pregna-1,4-diene-3,20-dione; Ercoli and Gardi, South African Patent No. 680,386, and Ercoli et al., US Patent No. 3,780,177);

5 enoxolone ((3 $\beta$ ,20 $\beta$ )-3-hydroxy-11-oxoolean-12-en-29-oic acid; British Patent No. 833,184), or its 18 $\alpha$ -hydrogen form; fluazacort ((11 $\beta$ ,16 $\beta$ )-21-(acetyloxy)-9-fluoro-11-hydroxy-2'-methyl-5'H-pregna-1,4-dieno[17,16-d]oxazole-3,20-dione; British Patent No. 1,119,082, and US Patent No. 3,461,119); flucoronide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-9,11-dichloro-6-fluoro-21-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-pregna-1,4-diene-3,20-dione; Bowers, US Patent No. 3,201,391); flumethasone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6,9-difluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione;

10 British Patent No. 902,292, and Lincoln et al., US Patent No. 3,499,016), its 21-acetate form (C<sub>24</sub>H<sub>30</sub>F<sub>2</sub>O<sub>6</sub>), or its 21-pivalate form (C<sub>27</sub>H<sub>36</sub>F<sub>2</sub>O<sub>6</sub>); flunisolide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione; British Patent No. 933,867, Ringold and Rosenkranz, US Patent No. 3,124,571, and Ringold et al., US Patent No. 3,126,375), or its 21-acetate form (C<sub>26</sub>H<sub>33</sub>FO<sub>7</sub>); fluocinolone acetate ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-pregna-1,4-diene-3,20-dione;

15 Mills and Bowers, US Patent No. 3,014,938, and Ringold et al., US Patent No. 3,126,375); fluocinonide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-21-(acetyloxy)-6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-pregna-1,4-diene-3,20-dione; British Patent No. 916,996, Ringold and Rosenkranz, US Patent No. 3,124,571, Ringold et al., US Patent No. 3,126,375, and Fried, US Patent No. 3,197,469); fluocortin butyl ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11-hydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-oic acid butyl ester; Laurent et al., German Patent Nos. 2,150,268 and

20 2,150,270, and US Patent No. 3,824,260); fluocortolone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione; Belgium Patent 614,196, and Kieslich et al., US Patent No. 3,232,839), its 21-acetate form (C<sub>24</sub>H<sub>31</sub>FO<sub>5</sub>), its 21-hexanoate form (C<sub>28</sub>H<sub>39</sub>FO<sub>5</sub>), or its 21-pivalate form (C<sub>22</sub>H<sub>37</sub>FO<sub>5</sub>); fluorometholone ((6 $\alpha$ ,11 $\beta$ )-9-fluoro-11,17-dihydroxy-6-methylpregna-1,4-diene-3,20-dione; Lincoln et al., US Patent No. 2,867,637), or its 17-acetate form (C<sub>24</sub>H<sub>31</sub>FO<sub>5</sub>; Magerlein et al., US Patent No. 3,038,914); fluperolone acetate ([11 $\beta$ ,17 $\alpha$ ,17(S)]-17-[2-(acetyloxy)-1-oxopropyl]-9-fluoro-11,17-dihydroxyandrost-1,4-dien-3-one; Agnello and Laubach, US Patent No. 3,234,095); fluprednidene acetate ((11 $\beta$ )-21-(acetyloxy)-9-fluoro-11,17-dihydroxy-16-methylenepregna-1,4-diene-3,20-dione; Wendler et al., US Patent Nos. 3,065,239, 3,068,224, 3,068,226 and 3,136,760); fluprednisolone ((6 $\alpha$ ,11 $\beta$ )-6-fluoro-11,17,21-trihydroxypregna-1,4-diene-3,20-dione; Batres et al., German Patent No. 1,079,042, and Lettre and Hotz, German Patent No. 1,088,953), or its 21-acetate form (C<sub>23</sub>H<sub>29</sub>FO<sub>6</sub>); flurandrenolide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregn-4-ene-3,20-dione; Ringold et

30 al., German Patent No. 1,131,213, and US Patent No. 3,126,375); fluticasone propionate ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ ,17 $\alpha$ )-6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)androst-1,4-diene-17-carbothioic acid S-(fluoromethyl) ester; Dutch Patent Application No. 8,100,707, and Phillipps et al., US Patent No. 4,335,121); formocortol ((11 $\beta$ ,16 $\alpha$ )-21-(acetyloxy)-3-(2-chloroethoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-20-

35 oxopregna-3,5-diene-6-carboxaldehyde; Camerino et al., France Patent No. 1,396,602, Dutch Patent Application No. 6,508,458, and US Patent No. 3,314,945); halcinonide ((11 $\beta$ ,16 $\alpha$ )-21-chloro-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregn-4-ene-3,20-dione; Difazio and Augustine, German Patent No. 2,355,710, and US Patent No. 3,892,857); halobetasol propionate (6 $\alpha$ ,11 $\beta$ ,16 $\beta$ )-21-chloro-6,9-difluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)pregna-1,4-diene-3,20-dione; Kalvoda and Anner, German Patent No. 2,743,069, and US Patent No.

40 4,619,921); halometasone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-2-chloro-6,9-difluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione; Anner et al., Dutch Patent Application No. 540,244, US Patent No. 3,652,554, and Swiss Patent No. 551,399), or its monohydrate form (C<sub>22</sub>H<sub>27</sub>ClF<sub>2</sub>O<sub>5</sub>•H<sub>2</sub>O); halopredone acetate ((6 $\beta$ ,11 $\beta$ )-17,21-bis(acetyloxy)-2-bromo-6,9-difluoro-11-hydroxypregna-1,4-diene-3,20-dione; Riva and Toscano, German Patent No. 2,508,136, and Riva et al., US Patent No. 4,226,862); hydrocortamate (N,N-diethylglycine (11 $\beta$ )-11,17-dihydroxy-3,20-

45 dioxopregn-4-en-21-yl ester; Pinson and Laubach, German Patent No. 1,016,708, and Richter and Schenck, German Patent No. 1,037,451), or its hydrochloride form (C<sub>27</sub>H<sub>41</sub>NO<sub>6</sub>•HCl); hydrocortisone ((11 $\beta$ )-11,17,21-trihydroxypregn-4-ene-3,20-dione; Murray and Peterson, US Patent No. 2,602,769), its 21-acetate form (C<sub>23</sub>H<sub>32</sub>O<sub>6</sub>), its 17-butyrate form (C<sub>25</sub>H<sub>36</sub>O<sub>6</sub>), its 21-phosphate disodium salt form (C<sub>21</sub>H<sub>29</sub>Na<sub>2</sub>O<sub>8</sub>P), its 21-sodium succinate form (C<sub>25</sub>H<sub>33</sub>NaO<sub>8</sub>), its 17-valerate form (C<sub>26</sub>H<sub>38</sub>O<sub>6</sub>), or its cypionate form (Munson and Wilson, J Pharm Sci (1981)

50 70(2), 177-81), examples of brand name for hydrocortisone include Cortef, Hydrocortone, examples of brand name for hydrocortisone cypionate include Cortef Oral Suspension; loteprednol etabonate ((11 $\beta$ ,17 $\alpha$ )-17-

[(ethoxycarbonyl)oxy]-11-hydroxy-3-oxoandrost-1,4-diene-17-carboxylic acid chloromethyl ester; Bodor, Belgium Patent No. 889,563, and US Patent No. 4,996,335); mazipredone ((11 $\beta$ )-11,17-dihydroxy-21-(4-methyl-1-piperazinyl)pregna-1,4-diene-3,20-dione; Tuba et al., Hungarian Patent No. 150,350), or its hydrochloride form (C<sub>26</sub>H<sub>38</sub>N<sub>2</sub>O<sub>4</sub>•HCl); medrysone ((6 $\alpha$ ,11 $\beta$ )-11-hydroxy-6-methylpregn-4-ene-3,20-dione; Sebek et al., US Patent No. 2,864,837, and Spero and Thompson, US Patent No. 2,968,655); meprednisone ((16 $\beta$ )-17,21-dihydroxy-16-methylpregna-1,4-diene-3,11,20-trione; British Patent No. 901,092, and Rausser and Oliveto, US Patent No. 3,164,618), or its 21-acetate form (C<sub>24</sub>H<sub>30</sub>O<sub>6</sub>); methylprednisolone ((6 $\alpha$ ,11 $\beta$ )-11,17,21-trihydroxy-6-methylpregna-1,4-diene-3,20-dione; Sebek and Spero, US Patent No. 2,897,218, and Gould, US Patent No. 3,053,832), its 21-acetate form (C<sub>24</sub>H<sub>32</sub>O<sub>6</sub>), its 21-phosphate disodium salt form (C<sub>22</sub>H<sub>29</sub>Na<sub>2</sub>O<sub>8</sub>P), its 21-succinate sodium salt form (C<sub>26</sub>H<sub>33</sub>NaO<sub>8</sub>), or its aceponate form (C<sub>27</sub>H<sub>36</sub>O<sub>7</sub>), examples of brand name for methylprednisolone include Medrol-Oral; mometasone furoate ((11 $\beta$ ,16 $\alpha$ )-9,21-dichloro-17-[(2-furanylcarbonyl)oxy]-11-hydroxy-16-methylpregna-1,4-diene-3,20-dione; Shapiro, European Patent Application No. 57,401, and US Patent No. 4,472,393); paramethasone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione; Edwards et al., J. Am.Chem.Soc. (1960) 82, 2318), its 21-acetate form (C<sub>24</sub>H<sub>31</sub>FO<sub>6</sub>), its disodium phosphate form, or a mixture of its 21-acetate and disodium phosphate form; prednicarbate ((11 $\beta$ )-17[(ethoxycarbonyl)oxy]-11-hydroxy-21-(1-oxopropoxy)pregna-1,4-diene-3,20-dione; Stache et al., Germany Patent No. 2,735,110, and US Patent No. 4,242,334); prednisolone ((11 $\beta$ )-11,17,21-trihydroxypregna-1,4-diene-3,20-dione; Nobile, US Patent Nos. 2,837,464 and 3,134,718), its 21-acetate form (C<sub>23</sub>H<sub>30</sub>O<sub>6</sub>), its 21-*tert*-butylacetate form (C<sub>27</sub>H<sub>38</sub>O<sub>6</sub>; Sarrett, US Patent No. 2,736,734), its 21-hydrogen succinate form (C<sub>25</sub>H<sub>32</sub>O<sub>8</sub>), its 21-succinate sodium salt form (C<sub>25</sub>H<sub>31</sub>NaO<sub>8</sub>; Shull and Kita, German Patent No. 1,045,400), its 21-stearoylglycolate form (C<sub>41</sub>H<sub>64</sub>O<sub>8</sub>; Giraldi and Nannini, US Patent No. 3,171,846), its 21-*m*-sulfobenzoate sodium salt form (C<sub>28</sub>H<sub>31</sub>NaO<sub>9</sub>S; (11 $\beta$ )-11,17-dihydroxy-21-[(3-sulfobenzoyl)oxy]pregna-1,4-diene-3,20-dione monosodium salt; Allais and Girault, US Patent No. 3,032,568, Joly and Warnant, US Patent No. 3,037,034), or its 21-trimethylacetate form (C<sub>26</sub>H<sub>36</sub>O<sub>6</sub>; Joly and Warnant, US Patent No. 3,037,034), examples of brand name for prednisolone include Prelone, Delta-Cortef, Pediapred, Adnisolone, Cortalone, Deltacortril, Deltasolone, Deltastab, Di-Adreson F, Encortolone, Hydrocortancyl, Medisolone, Meticortelone, Opredson, Panaafcortelone, Precortisyl, Prenisolone, Scherisolone, Scherisolone; prednisolone 21-diethylaminoacetate (N,N-diethylglycine (11 $\beta$ )-11,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl ester; British Patent No. 862,370), or its hydrochloride form (C<sub>27</sub>H<sub>39</sub>NO<sub>6</sub>•HCl); prednisolone sodium phosphate (11,17-dihydroxy-21-(phosphonooxy)pregna-1,4-diene-3,20-dione disodium salt; Sarett, US Patent No. 2,789,117, and Elks and Phillips, US Patent No. 2,936,313); prednisone (17,21-dihydroxypregna-1,4-diene-3,11,20-trione; Oliveto and Gould, US Patent No. 2,897,216, and Nobile, US Patent Nos. 2,837,464 and 3,134,718), or its 21-acetate form (C<sub>23</sub>H<sub>28</sub>O<sub>6</sub>), examples of brand name for prednisone include Deltasone, Liquid Pred, Meticorten, Orasone 1, Orasone 5, Orasone 10, Orasone 20, Orasone 50, Prednicen-M, Prednisone Intensol, Sterapred, Sterapred DS, Adasone, Cartancyl, Colisone, Cordrol, Cortan, Dacortin, Decorti, Decortisyl, Delcortin, Dellacort, Delta-Dome, Deltacortene, Deltisona, Diadreson, Econosone, Encorton, Fernisone, Nisona, Novoprednisone, Panafcort, Panasol, Paracort, Parmenison, Pehacort, Predeltin, Prednicort, Prednicot, Prednidib, Predniment, Rectodelt, Ultracorten, Winpred; prednival ((11 $\beta$ )-11,21-dihydroxy-17-[(1-oxopentyl)oxy]pregna-1,4-diene-3,20-dione; Ercoli and Gardi, US Patent No. 3,152,154), or its 21-acetate form (C<sub>28</sub>H<sub>38</sub>O<sub>7</sub>); prednylidene ((11 $\beta$ )-11,17,21-trihydroxy-16-methylenepregna-1,4-diene-3,20-dione; Mannhardt et al., Tetrahedron Letters (1960) 16, 21), or its 21-diethylaminoacetate hydrochloride form (C<sub>28</sub>H<sub>39</sub>NO<sub>6</sub>•HCl; German Patent No. 1,134,074); rimexolone ((11 $\beta$ ,16 $\alpha$ ,17 $\beta$ )-11-hydroxy-16,17-dimethyl-17-(1-oxopropyl)androst-1,4-dien-3-one; Dutch Patent Application No. 7,300,313, and Woods et al., US Patent No. 3,947,478); rofleponide ((22R)-6 $\alpha$ ,9 $\alpha$ -Difluoro-11 $\beta$ ,21-dihydroxy-16 $\alpha$ ,17 $\alpha$ -propylmethylenedioxypregn-4-ene-3,20-dione; Thalen and Wickstrom, Steroids (2000) 65(1), 16-23); tipredane ((11 $\beta$ , 17 $\alpha$ )-17-(ethylthio)-9 $\alpha$ -fluoro-11 $\beta$ -hydroxy-17-(methylthio) androst-1,4-dien-3-one; Wojnar et al., Arzneimittelforschung (1986) 36(12), 1782-7); tixocortol ((11 $\beta$ )-11,17-dihydroxy-21-mercaptopregn-4-ene-3,20-dione; Simons et al., J Steroid Biochem (1980) 13, 311), or its 21-pivalate form (C<sub>26</sub>H<sub>38</sub>O<sub>5</sub>S; (11 $\beta$ )-21-[(2,2-dimethyl-1-oxopropyl)thio]-11,17-dihydroxypregn-4-ene-3,20-dione; Torossian et al., German Patent No. 2,357,778, and US Patent No. 4,014,909); triamcinolone ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11,16,17,21-tetrahydroxypregna-1,4-diene-3,20-dione; Bernstein et al., US Patent No. 2,789,118, and Allen et al., US Patent No.3,021,347), or its 16,21-diacetate form (C<sub>25</sub>H<sub>31</sub>FO<sub>8</sub>; (11 $\beta$ ,16 $\alpha$ )-16,21-bis(acetyloxy)-9-fluoro-11,17-dihydroxypregna-1,4-diene-3,20-dione), examples of brand name for triamcinolone include Kenacort, Aristocort, Atolone, Sholog A, Tramacort-D, Tri-Med,

Triamcot, Tristo-Plex, Trylone D, U-Tri-Lone; Triamcinolone acetonide ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11,21-dihydroxy-16,17-[1-methylethylidenebis(oxy)]pregna-1,4-diene-3,20-dione; Bernstein and Allen, US Patent No. 2,990,401, and Hydrom, US Patent No. 3,035,050), its 21-acetate crystal form, its 21-disodium phosphate form (C<sub>24</sub>H<sub>30</sub>FN<sub>2</sub>O<sub>9</sub>P), or its 21-hemisuccinate form (C<sub>28</sub>H<sub>35</sub>FO<sub>9</sub>); triamcinolone benetonide ((11 $\beta$ ,16 $\alpha$ )-21-[3-(benzoylamino)-2-methyl-1-oxopropoxy]-9-fluoro-11-hydroxy-16,17-[1-methylethylidenebis(oxy)]pregna-1,4-diene-3,20-dione; Cavazza et al., German Patent No. 2,047,218, and US Patent No. 3,749,712); and triamcinolone hexacetonide ((11 $\beta$ ,16 $\alpha$ )-21-(3,3-dimethyl-1-oxobutoxy)-9-fluoro-11-hydroxy-16,17-[1-methylethylidenebis(oxy)]pregna-1,4-diene-3,20-dione; Nash and Naeger, US Patent No. 3,457,348). Preferably, the steroids comprises budesonide, testosterone, progesterone, estrogen, flunisolide, triamcinolone, beclomethasone, betamethasone, dexamethasone, fluticasone, methylprednisolone, prednisone, hydrocortisone, and mometasone. Another group of preferred steroids are mineralocorticoid steroids including aldosterone, deoxycorticosterone, deoxycorticosterone acetate and fludrocortisone. However, others are also suitable.

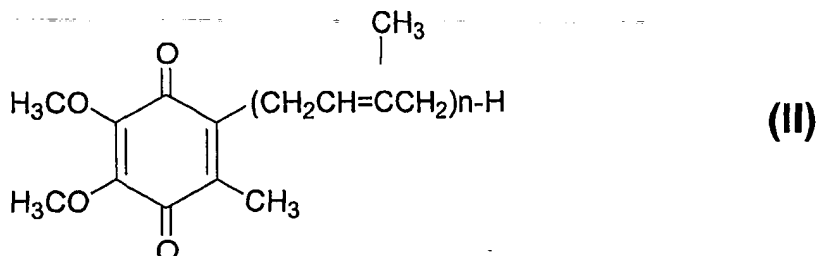
Also provided is a method for reducing or depleting adenosine levels, or treating hypersensitivity to adenosine, particularly in the lung, liver, heart and/or brain, or increasing levels of lung surfactant or of ubiquinone in the lung, heart or other tissues, and for treating various respiratory, lung and other diseases and their symptoms, by administering to a subject in need of such treatment a first active agent comprising the anti-sense oligo of the invention, and a second active agent comprising the AIS of chemical formula (Ia) and (Ib) exemplified by corticosteroids and dehydroepiandrosterones, analogues thereof, and pharmaceutically or veterinarily acceptable salts thereof, such as dehydroepiandrosterone sulfate (DHEA-S), and salts of the corticosteroids, and/or a ubiquinone of chemical formula (II) as described above, the active agents being present in amounts effective to reduce or deplete adenosine levels, or reduce adenosine hypersensitivity, or to increase lung surfactant levels or ubiquinone tissue levels, or to inhibit or control a variety of respiratory, lung and other diseases and conditions in the subject. Examples of non-glucocorticoid steroids that may be used to carry out this method are represented by the chemical formula (Ia) shown above.

Another group of preferred steroids for use in this invention are described below. The hydrogen atom at position 5 of the compound of chemical formula (Ia) may be present in the alpha or beta configuration, and the compound may comprise a mixture of both configurations. Compounds illustrative of compounds of chemical formula (I) above include DHEA, wherein R and R<sub>1</sub> each comprise hydrogen and the double bond is present; 16-alpha bromodehydroepiandrosterone, where R comprises Br, R<sub>1</sub> comprises H, and the double bond is present; 16-alpha-fluorodehydroepiandrosterone, wherein R comprises F, R<sub>1</sub> comprises H and the double bond is present; etiocholanolone, where R and R<sub>1</sub> each comprise hydrogen and the double bond is absent (the single bond is present); and dehydroepiandrosterone sulphate (DHEA-S), wherein R comprises H, R<sub>1</sub> comprises SO<sub>2</sub>OM and M comprises sulphatide as defined above, and the double bond is present, among others. In the compound of formula I, R preferably comprises halogen, e.g. bromo, chloro, or fluoro, R<sub>1</sub> comprises hydrogen, and the double bond is present. Most preferably the compound of Formula I comprises dehydroepiandrosterone sulphate and 16- $\alpha$ -fluorodehydroepiandrosterone. The compounds of formula I may be made in accordance with procedures known in the art, or employing variations thereof that will be apparent to those skilled in the art. See, for example, U.S. Patent No. 4,956,355, UK Patent No. 2,240,472, EPO Patent Application No. 429,187, Patent Publication WO9104030A1; Abou-Gharbia M. et al., J. Pharm. Sci. 70: 1154-1157 (1981), Merck Index Monograph No. 7710, 11th Ed. (1989). Other preferred non-glucocorticoid steroids are those of the formulas (III) and (IV), wherein R<sub>15</sub> and R<sub>16</sub> together are =O, or where R<sub>5</sub> is OH, or where R<sub>5</sub> is -OSO<sub>2</sub>R<sub>20</sub>, or where R<sub>20</sub> is H. Others, however, are also preferred and are encompassed by this patent.

"Corticosteroid", as used herein, means 21-carbon steroid hormone corticoids that bind to glucocorticoid receptors, having the chemical formula of (Ib). Corticosteroids are agonists for the glucocorticoid steroid receptor(s) and interact to promote a transcriptional response. The corticosteroids and other AIS may be used in conjunction with, and for reducing the amount of the oligo(s) employed for reducing inflammation and lung allergy(ies), reducing or depleting levels of, or reducing sensitivity to, adenosine, reducing adenosine receptor levels, producing bronchodilation, and/or for increasing levels of ubiquinone or lung surfactant in a subject, or for treating bronchoconstriction, lung inflammation or allergies or a respiratory or lung disease or condition. The anti-inflammatory steroid(s) may be administered per se or in the form of pharmaceutically acceptable salt, as discussed above. In general, the anti-inflammatory steroid(s), and its(their) salt(s) and crystal forms are suitable, and may be administered in a dosage of about 0.01, about 0.1, about 0.4, about 1, about 5, about 10, about 20 to about 4, about

30, about 70, about 100, about 300, about 1,000, about 3600 mg/kg body weight. These active compounds may be administered once or several times a day, or in any other regime, upon adjustment of the dose in accordance with the dosages of the other agents being administered.

The term "ubiquinone", as used herein, refers to a family of compounds having structures based on a  $\omega$  3-dimethoxy-5-methyl benzoquinone nucleus with a variable terpenoid acid chain containing on to twelve non-unsaturated trans-isoprenoid units. Such compounds are also known in the art as "Coenzyme Q<sub>n</sub>", wherein n comprises 1 to 12, preferably n comprising 1 to 10, and may be referred to herein as compounds represented by the following chemical formula



wherein n comprises 1 to 10. In the method of the invention, another preferred ubiquinone is a compound according to the above formula, where n comprises 6 to 10, i.e. Coenzyme Q<sub>6-10</sub>, and most preferably wherein n comprises 10, i.e. Coenzyme Q<sub>10</sub>.

As discussed above, the "active agents or compounds" may be administered per se or in the form of pharmaceutically acceptable salts, or in the same formulation with the other active agents of the invention, e.g. corticosteroid(s) and/or ubiquinone(s) and the anti-sense oligo, either systemically or topically. In general, they are administered in an amount effective to treat respiratory conditions including bronchoconstriction, respiratory inflammation and allergies, allergic rhinitis, pulmonary hypertension and fibrosis, apnea, sepsis, emphysema, cancers, asthma, COPD, RDS, CF, ARDS, and the like, and/or to off-set lung surfactant depletion or ubiquinone depletion in the lungs and/or heart of the subject if induced by the administration of the anti-inflammatory steroid of the invention. The ubiquinone is preferably administered in a total amount per day of about 0.1, about 1, about 5, about 10, about 15, about 30 to about 50, about 100, about 150, about 300, about 600, about 900, about 1200 mg/kg body weight per day. More preferred are about 1 to about 150 mg/kg, about 30 to about 100 mg/kg, and most preferred about 5 to about 50 mg/kg. The ubiquinone may be administered in one dose (once or several times a day), and its dose may be adjusted as is known in the art, depending on whether it is administered alone, or with the oligo and/or the anti-inflammatory steroid, and their amounts used. The dosage of the ubiquinone will vary depending upon the condition of the subject and route of administration. The ubiquinone may be administered by itself, or as a mixture of ubiquinones of varying side chain lengths, or concurrently, jointly prior to or subsequent to the anti-sense oligo and/or the anti-inflammatory steroid, for treating the overall symptoms described here, and/or the various diseases associated with them, including asthma, COPD, allergic rhinitis, pulmonary hypertension, vasoconstriction and fibrosis, and others described above. The phrase "concurrently administering", as used herein, means that the steroid, e. g. DHEA, DHEA-S or analogs of formulas (Ia) and (Ib), the anti-sense oligos, and the ubiquinone of chemical formula (II) are administered either (a) simultaneously in time, preferably by formulating the two active agents together in a common pharmaceutical carrier, or (b) at different times during the course of a common treatment schedule through the same or different routes of administration. In the latter case, for example the oligo may be administered once a week or its administration may be varied in accordance with its duration of action, while steroid(s) and ubiquinone(s) is(are) administered at times sufficiently close so that, in addition to its direct effect, the ubiquinone will be also off-setting any ubiquinone depletion in the subject's tissues, e. g. lungs and heart. This timing helps to prevent or counter-balance any deterioration of tissue, e. g. lung and heart, function that may result from the administration of the steroids or analogs thereof. Where the ubiquinone is formulated with a pharmaceutically acceptable carrier and other oral formulation components, it may be administered separately from the steroid and/or the oligo. For example, the steroid and the oligo may be administered into the respiration, by inhalation, nasally or into the lungs (by instillation) of the subject whereas the ubiquinone may be administered systemically. The ubiquinone may be formulated by any of the techniques set forth above.

The composition and formulations of this invention are highly efficacious for preventing and treating diseases and conditions associated with bronchoconstriction, difficult breathing, impeded and obstructed lung

airways, allergy(ies), inflammation and surfactant depletion, among others. Examples of diseases and conditions which are suitably treated by the present method are diseases and conditions, including Acute Respiratory Distress Syndrome (ARDS), asthma, adenosine administration e.g. in the treatment of SupraVentricular Tachycardia (SVT) and other arrhythmias, and in stress tests to hyper-sensitized individuals, ischemia, renal damage or failure induced by certain drugs, infantile respiratory distress syndrome, pain, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive pulmonary disease (COPD), lung transplantation rejection, pulmonary infections, and cancers such as leukemias, lymphomas, carcinomas, and the like, including colon cancer, breast cancer, lung cancer, pancreatic cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastases, etc., as well as all types of cancers which may metastasize or have metastasized to the lung(s), including breast and prostate cancer. The invention will be mostly described with respect to the adenosine receptors as targets, although data on other targets is also provided, but is similarly applicable to any other target including the listed targets, with respect to the administration of anti-sense oligos. The examples provided below show a complete inhibition of adenosine receptor associated symptoms in a rabbit model for human bronchoconstriction, allergy(ies) and inflammation as well as the elimination of the ability of the adenosine receptor agonist par excellence, adenosine, to cause bronchoconstriction in hyper-responsive monkeys, which are animal models for human hyper-responsiveness to adenosine receptor agonists. The pharmaceutical composition and formulations of the invention, therefore, are suitable for preventing and alleviating the symptoms associated with stimulation of adenosine receptors, such as the adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub>, and A<sub>3</sub> receptors, as well as other single or multiple targets. The compositions and formulations of this invention, thus, are also suitable for prevent the untoward side effects of adenosine-mediated hyperresponsiveness in certain individuals, which are generally seen in diseases affecting respiratory activity.

The method of the present invention may be used to treat airway and lung diseases and conditions in a subject of any kind and for any reason, for example, to reduced or eliminated with the intention that the adenosine content of anti-sense compounds, so as to prevent liberation of adenosine upon anti-sense degradation. Examples of diseases and conditions, which may be treated preventatively, prophylactically and therapeutically with the compositions and formulations of this invention, are pulmonary vasoconstriction, inflammation, allergies, asthma, allergic rhinitis, impeded respiration, Acute Respiratory Distress Syndrome (ARDS), renal damage and failure associated with ischemia as well as the administration of certain drugs, side effects associated with adenosine administration e.g. in SupraVentricular Tachycardia (SVT) and in adenosine stress tests, infantile Respiratory Distress Syndrome (infantile RDS), ARDS, pain, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive pulmonary disease (COPD), lung transplantation rejection, pulmonary infections, and cancers such as leukemias, lymphomas, carcinomas, and the like, e.g. colon cancer, breast cancer, lung cancer, pancreatic cancer, hepatocellular carcinoma, kidney cancer, melanoma, metastatic cancer such as hepatic metastases, lung, breast and prostate metastases, among others. The present compositions and formulations are suitable for administration before, during and after other treatments, including radiation, chemotherapy, antibody therapy, phototherapy and cancer, and other types of surgery. The present compositions and formulations may also be administered effectively as a substitute for therapies that have significant negative side effects. The terms "anti-sense" oligonucleotides generally refers to small, synthetic oligonucleotides, resembling single- and double-stranded DNA and RNA, which in this patent are applied to the inhibition of gene expression, e.g. by inhibition of a gene or target messenger RNA (mRNA). See, e.g. Milligan, J. F. et al., J. Med. Chem. 36(14), 1923-1937 (1993); Sharp, P.A. Genes & Development 15, 485-490, 2001; the relevant portion of which is hereby incorporated in its entirety by reference. For consistency's sake, all RNAs, DNAs and oligonucleotides are represented in this patent by a single strand in the 5' to 3' or 3' to 5' direction, when read from left to right, although their complementary and double-stranded sequence(s) is (are) also encompassed within the four corners of the invention. In addition, all nucleotide bases and amino acids are represented utilizing the recommendations of the IUPAC-IUB Biochemical Nomenclature Commission, or by the known 3-letter code (for amino acids). Nucleotide sequences are presented herein by single strand only, in the 5' to 3' direction, from left to right. In addition, nucleotide and amino acids are represented herein in the manner recommended by the IUPAC-IUB Biochemical Nomenclature Commission, or (for amino acids) by three letter code, in accordance with 37 CFR ' 1.822 and established usage. See, e.g., PatentIn User Manual, 99-102 (Nov. 1990) (U.S. Patent and Trademark Office, Office of the Assistant Commissioner for Patents, Washington, D.C. 20231); U.S. Patent No. 4,871,670 to Hudson et al. at col. 3, lines 20-43. The present method utilizes anti-sense agents to inhibit or down-regulate gene expression of

target genes, including those listed in Tables 1 and 2 below. This is generally attained by hybridization of the anti-sense oligonucleotides to coding (sense) sequences of a targeted messenger RNA (mRNA), as is known in the art. The oligos of this invention may be obtained by first selecting fragments of a target nucleic acid having at least 4 contiguous nucleic acids selected from the group consisting of G and C, and then obtaining a first oligonucleotide 4 to 70 nucleotides long which comprises the selected fragment and preferably has a C and G nucleic acid content of up to and including about 20%, about 15%. The oligonucleotide(s) (oligo(s)) may include at least one unmethylated cytosine-guanine (CpG) dinucleotide. The CpG dinucleotide may be substituted for a methylated cytosine present in the anti-sense oligonucleotide(s). The CpG dinucleotide is an immunostimulating sequence and affects the immune response in a subject by activating natural killer cells (NK) or redirecting a subject's immune response from a Th2 to a Th1 response by inducing monocytic and other cells to produce Th1 cytokines. The oligo(s) containing at least one unmethylated CpG can be used for treating and/or preventing respiratory and pulmonary diseases including bronchoconstriction, impaired airways, decreased lung surfactant, asthma, rhinitis, acute respiratory distress syndrome (ARDS), infantile or maternal RDS, chronic obstructive pulmonary disease (COPD), allergies, impeded respiration, lung pain, cystic fibrosis (CF), infectious diseases, cancers such as leukemias, lung and colon cancer, and the like, and diseases whose secondary effects afflict the lungs. A "CpG" or "CpG motif" refers to nucleotides having a cytosine followed by a guanine linked by a phosphate bond. The term "methylated CpG" refers to the methylation of the cytosine on the pyrimidine ring, usually occurring the 5-position of the pyrimidine ring. The term "unmethylated CpG" refers to the absence of methylation of the cytosine on the pyrimidine ring. Methylation, partial removal, or removal of an unmethylated CpG motif in an oligo(s) is believed to reduce its effect. Methylation or removal of all unmethylated CpG motifs in an oligo(s) substantially reduces its effect. The effect of methylation or removal of a CpG motif is "substantial" if the effect is similar to that of an oligonucleotide that does not contain a CpG motif. Preferably the CpG oligonucleotide is in the range of about 8 to 30 bases in size. The oligo(s) can be synthesized de novo using any of a number of procedures well known in the art. For example, the b-cyanoethyl phosphoramidite method (Beaucage, S. L., and Caruthers, M. H., Tet. Let. 22:1859, 1981); nucleoside H-phosphonate method (Garegg et al., Tet. Let. 27:4051-4054, 1986; Froehler et al., Nucl. Acid. Res. 14:5399-5407, 1986; Garegg et al., Tet. Let. 27:4055-4058, 1986, Gaffney et al., Tet. Let. 29:2619-2622, 1988). These chemistries can be performed by a variety of automated oligonucleotide synthesizers available in the market. Alternatively, CpG dinucleotides can be produced on a large scale in plasmids, (see Sambrook, T., et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor laboratory Press, New York, 1989) which after being administered to a subject are degraded into an oligo(s). An oligo(s) can be prepared from existing nucleic acid sequences (e.g., genomic or cDNA) using known techniques, such as those employing restriction enzymes, exonucleases or endonucleases. The exogenously administered agents of the invention decrease the levels of mRNA and protein encoded by the target gene and/or cause changes in the growth characteristics or shapes of the thus treated cells. See, Milligan et al. (1993); Helene, C. and Toulme, J. Biochim. Biophys. Acta 1049, 99-125 (1990); Cohen, J. S. D., Ed., Oligodeoxynucleotides as Anti-sense Inhibitors of Gene Expression; CRC Press: Boca Raton, FL (1987), the relevant portion of which is hereby incorporated in its entirety by reference.

The treatment of this invention enhances the effects of the oligonucleotide and the anti-inflammatory steroid(s) and/or ubiquinone(s) by combining them, either simultaneously, sequentially or separately, for reducing or depleting levels of, or reducing sensitivity to, adenosine, reducing levels of receptor(s), producing bronchodilation, or for increasing levels of ubiquinone or lung surfactant in a subject's tissue (s), or treating bronchoconstriction, lung inflammation or allergies or a respiratory or lung disease or condition, and/or for alleviating bronchoconstriction or lung inflammation or allergy(ies), or ubiquinone or lung surfactant depletion or hyposecretion, in a subject. When administered in combination, the dose of the oligonucleotide or the steroid(s) or ubiquinone(s) may be decreased since they potentiate each other's effect. These agents may be administered before, simultaneously with, and/or after each other's administration. Accordingly, the details of administration of the effect enhancer including its amount, route, formulation, method, target organ and/or tissue may be determined as described throughout this specification. Similarly, other therapeutic or bioactive agents may be employed in accordance with this invention. Kits comprising the various agents described above are also part of this invention.

As used herein, "anti-sense oligonucleotide or anti-sense oligo" is generally a short sequence of synthetic nucleotide that hybridizes to any segment of a mRNA encoding a targeted protein under appropriate hybridization conditions and which, upon hybridization, causes a decrease in gene expression of the targeted protein. The terms "desAdenosine" (desA), "des-thymidine" (desT) and "des-uridine (desU) refer to oligonucleotides substantially



lacking either adenosine (desA) or thymidine (desT) (uracil (desU)). In some instances, the desA or desT (desU) sequences are naturally occurring, and in others they may result from substitution of an undesirable nucleotide (A) by another lacking its undesirable activity, such as acting as an agonist or having a triggering effect at the adenosine A receptor(s). In the present context, the substitution is generally accomplished by substitution of A with a "universal or alternative base", presently known in the art or to be ascertained at a later time. As used herein, the terms "prevent", "preventing", "treat" or "treating" refer to a preventative, prophylactic, maintenance, or therapeutic treatment which decreases the likelihood that the subject administered such treatment will manifest symptoms associated with adenosine receptor stimulation. The term "down-regulate" refers to inducing a decrease in production, secretion or availability and, thus, a decrease in concentration, of intracellular target product, be it a receptor, e. g. adenosine A<sub>1</sub>, A<sub>2b</sub>, A<sub>3</sub>, bradykinin 2B, GATA-3, or other receptors, or produce a stimulatory effect on a receptor such as the adenosine A<sub>2a</sub> receptor. The present technology relies on the design of anti-sense oligos targeted to genea and mRNAs associated with ailments involving nasal and lung airway(s) (respiratory tract) pathology(ies), and on their modification to reduce the potential occurrence of undesirable side effects caused by their release of adenosine upon breakdown, while preserving their activity and efficacy for their intended purpose. In this manner, the inventor targets a specific gene to design one or more anti-sense single or double stranded DNA or RNA oligonucleotide(s) (oligos) that selectively bind(s) to the corresponding gene or mRNA, and then reduces, if necessary, their content of adenosine via substitution with an alternative or a universal base, or an adenosine analog incapable of significantly, or having substantially reduced ability for, activating or antagonizing adenosine A<sub>1</sub>, A<sub>2b</sub> or A<sub>3</sub> receptors or which may act as an agonist at the adenosine A<sub>2a</sub> receptor. Any number of adenosines present may be substituted by an alternative and/or universal base, such as heteroaromatic bases, which binds to a thymidine or uridine base but has less than about 0.3 of the adenosine base agonist or antagonist activity at the adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub> and A<sub>3</sub> receptors. Based on his prior experience in the field, the inventor reasoned that in addition to "downregulating" specific genes, he could increase the effect of the agent(s) administered by either selecting segments of RNA that are devoid, or have a low content, of thymidine (T) or uridine (U), or alternatively, substitute one or more adenosine(s) present in the designed oligonucleotide(s) with other nucleotide bases, so called universal bases, which bind to thymidine but lack the ability to activate adenosine receptors and otherwise exercise the constricting effect of adenosine in the lungs, etc. Given that adenosine (A) is a nucleotide base complementary to thymidine (T) or uridine (U), wherein when a U appears in the RNA, the anti-sense oligo will have an A at the same position.

In one aspect of this invention, the anti-sense oligonucleotide has a sequence which specifically binds to a portion or segment of a mRNA molecule which encodes or regulates the production of a protein associated with impeded breathing, allergy(ies), lung inflammation, depletion of lung surfactant or lowering of lung surfactant, airway obstruction, bronchitis, and the like. One effect of this binding is to reduce or even prevent the translation of the corresponding mRNA and, thereby, reduce the available amount of target protein in the subject's lung. In one preferred embodiment of this invention, the phosphodiester residues of the anti-sense oligonucleotide are modified or substituted. Chemical analogs of oligonucleotides with modified or substituted phosphodiester residues, e.g., to the methylphosphonate, the phosphotriester, the phosphorothioate, the phosphorodithioate, or the phosphoramidate, 2' methoxy ethyl and similar modifications, which increase the in vivo stability of the oligonucleotide are particularly preferred. The naturally occurring phosphodiester linkages of oligonucleotides are susceptible to some degree of degradation by cellular nucleases. Many of the residues proposed herein, on the contrary, are highly resistant to nuclease degradation. See, Milligan et al.; Cohen, J. S. D., *supra*. In another preferred embodiment of the invention, the oligonucleotides may be protected from degradation by adding a "3'-end cap" by which nuclease-resistant linkages are substituted for phosphodiester linkages at the 3' end of the oligonucleotide. See, Tidd, D. M. and Warenus, H.M., *Be. J. Cancer* 60: 343-350 (1989); Shaw, J.P. et al., *Nucleic Acids Res.* 19: 747-750 (1991), the relevant section of which are incorporated in their entireties herein by reference. Phosphoramidates, phosphorothioates, and methylphosphonate linkages all function adequately in this manner for the purposes of this invention, as do 2' modifications, such as 2' methoxy ethyl, and the like. The more extensive the modification of the phosphodiester backbone the more stable the resulting agent, and in many instances the higher their RNA affinity and cellular permeation. See, Milligan, et al., *supra*. In addition, a plurality of substitutions to the carbohydrate ring are also known to improve stability of nucleic acids. Thus, the number of residues which may be modified or substituted will vary depending on the need, target, and route of administration, and may be from 1 to all the residues, to any number in between. Many different methods for replacing the entire phosphodiester backbone with



novel linkages are known. See, Millikan et al, supra. Preferred backbone analogue residues include phosphoramidate, phosphorothioate, methylphosphonate, phosphotriester, phosphotriester, thioformacetal, phosphorodithioate, phosphoramidate, formacetal, triformacetal, thioether, carbamate, boranophosphate, 3'-thioformacetal, 5'-thioether, carbonate, C<sub>5</sub>-substituted nucleotides, 5'-N-carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, 2'-O methyl, sulfoxide, sulfide, hydroxylamine, methylene(methylimino) (MMI), methoxymethyl (MOM), and methoxyethyl (MOE), and methyleneoxy(methylimino) (MOMI) residues, and combinations thereof. Phosphorothioate and methylphosphonate-modified oligonucleotides are particularly preferred due to their availability through automated oligonucleotide synthesis. See, Millikan et al, supra. Where appropriate, the agent of this invention may be administered in the form of their pharmaceutically acceptable salts, or as a mixture of the anti-sense oligonucleotide and its salt. In another embodiment of this invention, a mixture of different anti-sense oligonucleotides or their pharmaceutically acceptable salts is administered. A single agent of this invention has the capacity to attenuate the expression of a target mRNA and/or various agents to enhance or attenuate the activity of a pathway. By means of example, the present method may be practiced by identifying all possible deoxyribonucleotide segments which are low in thymidine (T), ribonucleotides that are low in uridine (U), or deoxynucleotide segments low in adenosine (A) of about 7 or more mononucleotides, preferably up to about 60 mononucleotides, more preferably about 10 to about 36 mononucleotides, and still more preferably about 12 to about 21 mononucleotides, in a target mRNA or a gene, respectively. This may be attained by searching for nucleotide segments within a target sequence which are low in, or lack thymidine (DNA) or uridine (RNA), a nucleotide which is complementary to adenosine, or that are low in adenosine (gene), that are 7 or more nucleotides long. In most cases, this search typically results in about 10 to 30 such sequences, i.e. naturally lacking or having less than about 40% adenosine, anti-sense oligonucleotides of varying lengths for a typical target mRNA of average length, i.e., about 1800 nucleotides long. Those with high content of T, U or A, respectively, may be fixed by substitution of a universal base for one or more As. The agent(s) of this invention may be of any suitable length, including but not limited to, about 7 to about 60 nucleotides long, preferably about 12 to about 45, more preferably up to about 30 nucleotides long, and still more preferably up to about 21, although they may be of other lengths as well, depending on the particular target and the mode of delivery. The agent(s) of the invention may be directed to any and all segments of a target RNA. One preferred group of agent(s) includes those directed to an mRNA region containing a junction between an intron and an exon. Where the agent is directed to an intron/exon junction, it may either entirely overlie the junction or it may be sufficiently close to the junction to inhibit the splicing-out of the intervening exon during processing of precursor mRNA to mature mRNA, e.g. with the 3' or 5' terminus of the anti-sense oligonucleotide being positioned within about, for example, within about 2 to 10, preferably about 3 to 5, nucleotide of the intron/exon junction. Also preferred are anti-sense oligonucleotides which overlap the initiation codon, and those near the 5' and 3' termini of the coding region. The flanking regions of the exons may also be targeted as well as the spliced segments in the precursor mRNAs. The mRNA sequences of the adenosine receptors and of many other targets are derived from the DNA base sequence of the gene expressing either receptors, e. g. the adenosine receptors, the enzymes, factors, or other targets associated with airway disease. For example, the sequence of the genomic human A<sub>1</sub> adenosine receptor is known and is disclosed in U.S. Patent No. 5,320,963 to Stiles, G., et al. The A<sub>3</sub> adenosine receptor has been cloned, sequenced and expressed in rat (see, Zhou, F., et al., P.N.A.S. (USA) 89: 7432 (1992)) and human (see, Jacobson, M. A., et al., U.K. Patent Application No. 9304582.1 (1993)). The sequence of the adenosine A<sub>2b</sub> receptor gene is also known. See, Salvatore, C. A., Luneau, C. J., Johnson, R. G. and Jacobson, M., Genomics (1995), the relevant portion of which is hereby incorporated in its entirety by reference. The sequences of many of the remaining exemplary target genes are also known. See, GenBank, NIH. The sequences of those genes whose sequences are not yet available may be obtained by isolating the target segments applying technology known in the art. Once the sequence of the gene, its RNA and/or the protein are known, an anti-sense oligonucleotides may be produced according to this invention as described above to reduce the production of the targeted protein in accordance with standard techniques. The sequences for the adenosine A<sub>2a</sub> bradykinin, and other genes as well as methods for preparation of oligonucleotides are also known as those of many other target genes and mRNAs for which this invention is suitable. Thus, anti-sense oligonucleotides that downregulate the production of target sequences associated with airway disease, including the adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub>, A<sub>3</sub>, bradykinin, GATA-3, COX-2, and many other receptors, may be produced in accordance with standard techniques. Examples of diseases and conditions which are suitably treated by the present method are diseases and conditions, including Acute Respiratory Distress Syndrome (ARDS), asthma, adenosine administration e.g. in the

treatment of SupraVentricular Tachycardia (SVT) and other arrhythmias, and in stress tests to hyper-sensitized individuals, ischemia, renal damage or failure induced by certain drugs, infantile respiratory distress syndrome, pain, cystic fibrosis, pulmonary hypertension, pulmonary vasoconstriction, emphysema, chronic obstructive pulmonary disease (COPD), pulmonary transplantation rejection, pulmonary infections, and cancers such as leukemias, lymphomas, carcinomas, and the like, including colon cancer, breast cancer, lung cancer, pancreatic cancer, hepatocellular carcinoma, kidney cancer, melanoma, hepatic metastases, etc., as well as all types of cancers which may metastasize or have metastasized to the lung(s), including breast and prostate cancer.

The adenosine receptors discussed above are mere examples of the high power of the inventor's technology. In fact, a large number of genes may be targeted in a similar manner by the present agent(s), to reduce or down-regulate protein expression. This targeting may be attained by selecting a single target, or multiple targets. In the latter case, the oligos targeted to different sequences may be mixed for their administration or they may be multiple targeted anti-sense oligos (MTAs) in accordance with one embodiment of this invention; that is, the MTA sequence binds to more than one target polynucleotide, be it DNA or RNA. By means of example, if the target disease or condition is one associated with impeded or reduced breathing, bronchoconstriction, chronic bronchitis, pulmonary bronchoconstriction and/or hypertension, chronic obstructive pulmonary disease (COPD), pulmonary transplantation rejection, pulmonary infections, allergy, asthma, cystic fibrosis, respiratory distress syndrome, cancers, which either directly or by metastasis afflict the lung, the present method may be applied to a list of potential target mRNAs, which includes the targets listed in Table 1 and Table 2 below, among others. The anti-sense agent(s) of the invention have a low A content to prevent its liberation upon in vivo degradation of the agent(s). For example, if the system is the pulmonary or respiratory system, a large number of genes is involved in different functions, including those listed in Table 1 below.

**Table 1: Pulmonary and Inflammatory Targets**

NFκB Transcription Factor	Interleukin-8 Receptor (IL-8 R)
Interleukin-5 Receptor (IL-5R)	Interleukin-4 Receptor (IL-4R)
Interleukin-3 Receptor (IL-3R)	Interleukin-1β (IL-1β)
Interleukin-1β Receptor (IL-1βR)	Eotaxin
Tryptase	Major Basic Protein
β2-adrenergic Receptor Kinase	Endothelin Receptor A
Endothelin Receptor B	Preproendothelin
Bradykinin B2 Receptor (B2BR)	IgE (High Affinity Receptor)
Interleukin-1 (IL-1)	Interleukin 1 Receptor (IL-1 R)
Interleukin-9 (IL-9)	Interleukin-9 Receptor (IL-9 R)
Interleukin-11 (IL-11)	Interleukin-11 Receptor (IL-11 R)
Inducible Nitric Oxide Synthase	Cyclooxygenase (COX)
Intracellular Adhesion Molecule 1 (ICAM-1)	Vascular Cellular Adhesion Molecule (VCAM)
Substance P	Endothelial Leukocyte Adhesion Molecule Endothelin ETA Receptor (ELAM-1)
Rantes	GM-CSF, Endothelin-1
Cyclooxygenase-2 (COX-2)	Neutrophil Chemotactic Factor
Monocyte Activating Factor	Defensin 1,2,3
Neutrophil Elastase	Platelet Activating Factor
Muscarinic Acetylcholine Receptors	5-lipoxygenase
Tumor Necrosis Factor α	Substance P
Phosphodiesterase IV	Histamine Receptor
Substance P Receptor	CCR-1 CC Chemokine Receptor
Chymase	Interleukin-4 (IL-4)
Interleukin-2 (IL-2)	Interleukin-5 (IL-5)
Interleukin-12 (IL-12)	Interleukin-7 (IL-7)
Interleukin-6 (IL-6)	Interleukin-12 Receptor (IL-12R)
Interleukin-8 (IL-8)	Interleukin-1 (IL-1)
Interleukin-7 Receptor (IL-7R)	

	Interleukin-14 Receptor (IL-14R)	Interleukin-14
	CCR-2 CC Chemokine Receptor	CCR-3 CC Chemokine Receptor
	CCR-4 CC Chemokine Receptor	CCR-5 CC Chemokine Receptor
	Prostanoid Receptors	GATA-3 Transcription Factor
5	Neutrophil Adherence Receptor	MAP Kinase
	Interleukin-15 (IL-15)	Interleukin-15 Receptor (IL-15R)
	Interleukin-11 (IL-11)	Interleukin-11 Receptor (IL-11R)
	NFAT Transcription Factors	STAT 4
	MIP-1 $\alpha$	MCP-2
10	MCP-3	MCP-4
	Cyclophilin (A, B, etc.)	Phospholipase A2
	Basic Fibroblast Growth Factor	Metalloproteinase
	CSBP/p38 MAP Kinase	Tryptase Receptor
	PDG2	Interleukin-3 (IL-3)
15	Interleukin-10 (IL-10)	Cyclosporin A - Binding Protein
	FK506-Binding Protein	$\alpha 4\beta 1$ Selectin
	Fibronectin	$\alpha 4\beta 7$ Selectin
	cMad CAM-1	LFA-1 (CD11a/CD18)
	PECAM-1	LFA-1 Selectin
20	C3bi	PSGL-1
	E-Selectin	P-Selectin
	CD-34	L-Selectin
	p150,95	Mac-1 (CD11b/CD18)
	Fucosyl transferase	VLA-4
25	STAT-1	STAT-2
	CD-18/CD11a	CD11b/CD18
	ICAM2 and ICAM3	C5a
	CCR3 (Eotaxin Receptor)	CCR1, CCR2, CCR4, CCR5
	LTB-4	AP-1 Transcription Factor
30	Protein kinase C	Cysteinyl Leukotriene Receptor
	Tachykinin Receptors (tach R)	I $\kappa$ B Kinase 1 & 2
	Interleukin-2 Receptor (IL-2R)	(e.g., Substance P, NK-1 & NK-3 Receptors)
	STAT 6	c-mas
	NF-Interleukin-6 (NF-IL-6)	Interleukin-10 Receptor (IL-10R)
35	Interleukin-3 (IL-3)	Interleukin-2 Receptor (IL-2R)
	Interleukin-13 (IL-13)	Interleukin-12 Receptor (IL-12R)
	Interleukin-14 (IL-14)	Interleukin-6 Receptor (IL-6R)
	Interleukin-16 (IL-16)	Interleukin-13 Receptor (IL-13R)
	Medullasin	Interleukin-16 Receptor (IL-16R)
40	Adenosine A <sub>1</sub> Receptor (A <sub>1</sub> R)	Tryptase-I
	Adenosine A <sub>2b</sub> Receptor (A <sub>2b</sub> R)	Adenosine A <sub>3</sub> Receptor (A <sub>3</sub> R)
	$\beta$ Tryptase	STAT-3
	Adenosine A <sub>2a</sub> Receptor (A <sub>2a</sub> R)	IgE Receptor $\beta$ Subunit (IgE R $\beta$ )
	Fc-epsilon receptor CD23 antigen	IgE Receptor $\alpha$ Subunit (IgE R $\alpha$ )
45	IgE Receptor Fc Epsilon Receptor (IgERFc $\xi$ R)	Substance P Receptor
	Histidine decarboxylase	Tryptase-1
	Prostaglandin D Synthase	Eosinophil Cationic Protein
	Eosinophil Derived Neurotoxin	Eosinophil Peroxidase
	Endothelial Nitric Oxide Synthase	Endothelial Monocyte Activating Factor
50	Neutrophil Oxidase Factor	Cathepsin G
	Macrophage Inflammatory Protein-1-	Interleukin-8 Receptor $\alpha$ Subunit (IL-8 R $\alpha$ )
	Alpha/Rantes Receptor	Endothelin Receptor ET-B

- H2A histone family, member N      Tubulin, beta polypeptide
- ELL gene (11-19 lysine-rich leukemia gene)      7-dehydrocholesterol reductase
- ADP-ribosylation factor-like 7      Karyopherin alpha 2 (RAG cohort 1, importin alpha 1)
- EST (AI038433)      EST (AI122689)
- 5 EST (AI092623)      ESTs (AI095492)
- ESTs (AI138216)      ESTs (AI128305)
- ESTs (AI125228)      ESTs (AI041482)
- ESTs (AI051839)      Homo sapiens mRNA; cDNA DKFZp434A1716
- ESTs (AI096522)      ESTs (AI122807)
- 10 ESTs (AI041212)      EST (AI125651)
- Enolase 1, (alpha)      EST (AI024215)
- EST (AI034360)      Homo sapiens mRNA; cDNA DKFZp564H0764
- Homo sapiens mRNA for KIAA1363 protein, partial cds
- Potassium voltage-gated channel, shaker-related subfamily, beta member 2
- 15 ER-associated DNAJ; ER-associated Hsp40 co-chaperone; hDj9; ERj3
- ESTs, Weakly similar to p38 protein [H.sapiens] (AA906703)
- CGI-142      ESTs (AA463249)
- Homo sapiens clone 25058 mRNA sequence ESTs (R49144)
- Squamous cell carcinoma antigen 1      ESTs (AA425700)
- 20 Myosin X      ESTs (AA459692)
- Epithelial protein lost in neoplasm beta      CD44 antigen (homing function and Indian blood group system)
- Coagulation factor III (thromboplastin, tissue factor)
- ESTs (AA909635)      Adducin 1 (alpha)
- 5' Nucleotidase (CD73)
- 25 ESTs, Moderately similar to semaphorin C [M.musculus] (AA293300)
- ESTs (AA278764)      ESTs (AA678160)
- Calmodulin 2 (phosphorylase kinase, delta)      ESTs (R42770)
- Chloride intracellular channel 1      High-mobility group (nonhistone chromosomal) protein 17
- Ubiquitin carrier protein      Tubulin, alpha 1 (testis specific)
- 30 Transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)
- Sparc/osteonectin, cwcw and kazal-like domains proteoglycan (testican)
- Proteasome (prosome, macropain) 26S subunit, non-ATPase, 2
- Tubulin, beta polypeptide      Filamin B, beta (actin-binding protein-278)
- Stanniocalcin
- 35 Low density lipoprotein receptor (familial hypercholesterolemia)
- Plectin 1, intermediate filament binding protein, 500kD
- S100 calcium-binding protein A2      Immediate early response 3
- Calpain, large polypeptide L2      Pleckstrin homology-like domain, family A, member 1
- Melanoma adhesion molecule
- 40 CD44 antigen (homing function and Indian blood group system)
- Programmed cell death 5      Hexokinase 1
- Vascular endothelial growth factor      Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)
- Calumenin      Syntaxin 11
- Diphtheria toxin receptor (heparin-binding epidermal growth factor-like growth factor)
- 45 Fn14 for type I transmembrane protein      Nef-associated factor 1
- High-mobility group (nonhistone chromosomal) protein isoforms I and Y
- Catechol-O-methyltransferase      C-terminal binding protein 1
- Collagen, type XVII, alpha 1      ESTs (N58473)
- Farnesyl-diphosphate farnesyltransferase 1      RNA helicase-related protein
- 50 Interferon stimulated gene (20kD)
- Steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)
- Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)

Laminin, alpha 3 (nicein (150kD), kalinin (165kD), BM600 (150kD), epilegrin)

Collagen, type XVII, alpha 1                      Keratin 18

**Heparan sulfate (glucosamine) 3-O-sulfotransferase 1**

Tubulin, alpha 2                      Adenylyl cyclase-associated protein

5 Forkhead box D1 Cathepsin C

ESTs, Highly similar to AF151802 1 CGI-44 protein [H.sapiens] (T74688)

Ribonucleotide reductase M2 polypeptide

Laminin, gamma 2 (nicein (100kD), kalinin (105kD), BM600 (100kD), Herlitz junctional epidermolysis bullosa))

Homo sapiens mRNA: cDNA DKFZp586P1622 (from clone DKFZp586P1622)

10 ESTs, Weakly similar to /prediction (AA284245)

**Lactate dehydrogenase A**

Note that in the parantheses after "EST(s)" is GENABNK ACESSION NO.

These genes, and others, are involved in the normal functioning of respiration as well as in diseases associated with respiratory pathologies, including cystic fibrosis, asthma, pulmonary hypertension and vasoconstriction, chronic obstructive pulmonary disease (COPD), pulmonary transplantation rejection, pulmonary infections, chronic bronchitis, respiratory distress syndrome (ARDS), allergic rhinitis, lung cancer and lung metastatic cancers and other airway diseases, including those with inflammatory response.

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metastatic cancers and other airway diseases, including those with inflammatory response.

Anti-sense oligos to the target receptors, e. g. the adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub>, and A<sub>3</sub> receptors, CCR3 (chemokine receptors), bradykinin 2B, VCAM (vascular cell adhesion molecule), and eosinophil receptors, among others, have been shown to be effective in down-regulating the expression of their genes. Some of these act to alleviate the symptoms or reduce respiratory ailments and/or inflammation, for example, by “down regulation” of the adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub>, and/or A<sub>3</sub> receptors and CCR3, bradykinin 2B, VCAM (vascular cell adhesion molecule) and eosinophil receptors. These agents may be utilized by the present method alone or in conjunction with anti-sense oligos targeted to other genes to validate pathway and/or networks in which they are involved. For better

20 others, have been shown to be effective in down-regulating the expression of their genes. Some of these act to alleviate the symptoms or reduce respiratory ailments and/or inflammation, for example, by “down regulation” of the adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub>, and/or A<sub>3</sub> receptors and CCR3, bradykinin 2B, VCAM (vascular cell adhesion molecule) and eosinophil receptors. These agents may be utilized by the present method alone or in conjunction with anti-sense oligos targeted to other genes to validate pathway and/or networks in which they are involved. For better

25 results, the oligos are preferably administered directly into the respiratory system, e.g., by inhalation or other means, of the experimental animal, so that they may reach the lungs without widespread systemic dissemination. This permits the use of low agent doses as compared with those administered systemically or by other generalized routes and, consequently, reduces the number and degree of undesirable side effects resulting from the agent's widespread distribution in the body. The agent(s) of this invention has (have) been shown to reduce the amount of receptor

protein expressed by the tissue. These agents, thus, rather than merely interacting with their targets, e.g. a receptor, lower the number of target proteins that other drugs may interact with. In this manner, the present agent(s) afford(s) extremely high efficacy with low toxicity. Anti-sense oligonucleotides to the A<sub>1</sub>, A<sub>2b</sub>, A<sub>3</sub>, bradykinin B<sub>2</sub>, GATA-3, VCAM (vascular cell adhesion molecule), eosinophil receptors, and COX-2 receptors, among others, have been shown to be effective in the down-regulation of the respective receptor proteins in the cell. One novel feature of this

35 treatment, as compared to traditional treatments for adenosine-mediated bronchoconstriction, is that administration is direct to the lungs, or in situ to other tissues, organs or systems of the body. Additionally, a receptor protein itself is reduced in amount, rather than merely interacting with a drug, and toxicity is reduced. Other proteins that may be targeted with anti-sense agents for the treatment of lung conditions include, but are not limited to: CCR3 (chemokine) receptors, human A<sub>2A</sub> adenosine receptor, human A<sub>2B</sub> adenosine receptor, human IgE receptor  $\beta$ , human

40 Fc-epsilon receptor CD23 antigen, human histidine decarboxylase, human beta tryptase, human tryptase-I, human prostaglandin D synthase, human cyclooxygenase-2, human eosinophil cationic protein, human eosinophil derived neurotoxin, human eosinophil peroxidase, human intercellular adhesion molecule-1 (ICAM-1), human vascular cell adhesion molecule-1 (VCAM-1), human endothelial leukocyte adhesion molecule-1 (ELAM-1), human P selectin, human endothelial monocyte activating factor human II-3 human II-4 human II-5 human II-6 human II-8

45 human monocyte-derived neutrophil chemotactic factor, human neutrophil elastase, human neutrophil oxidase factor, human cathepsin G, human defensin 3, human defensin 3, human macrophage inflammatory protein-1-alpha, human muscarinic acetylcholine receptor HM3, human fibronectin, human GM-CSF, human tumor necrosis factor  $\alpha$ , human leukotriene C4 synthase, human major basic protein, and human endothelin 1. Although not intended to be exclusive, a more extensive list of genes and sequences are provided below. Some of these act to alleviate the

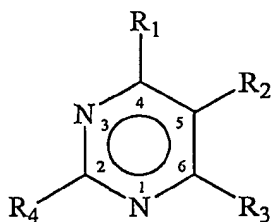
50 symptoms or reduce respiratory ailments and/or inflammation, for example, by "down regulation" of the adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub>, and/or A<sub>3</sub> receptors and CCR3, bradykinin 2B, VCAM (vascular cell adhesion molecule) and eosinophil receptors. These agents are preferably administered directly into the respiratory system, e.g., by

inhalation or other means, so that they may reach the lungs without widespread systemic dissemination. This permits the use of substantially lower doses of the agent of the invention as compared with those administered by the prior art, systemically or by other generalized routes and, consequently, reduce undesirable side effects resulting from the agent's widespread distribution in the body. The agent(s) of this invention has (have) been shown to reduce the amount of receptor protein expressed by the tissue. These agents, thus, rather than merely interacting with their targets, e.g. a receptor, lower the number of target proteins that other drugs may interact with. In this manner, the present agent(s) afford(s) extremely high efficacy with low toxicity. In these latter targets, and in target genes in general, it is particularly imperative to eliminate or reduce the adenosine content of the corresponding anti-sense oligonucleotide to prevent their breakdown products from liberating adenosine.

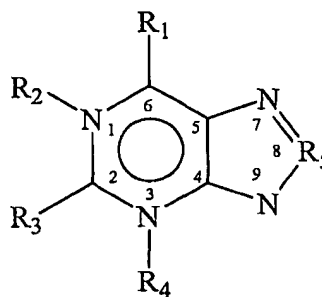
As used herein, the term "treat" or "treating" refers to a treatment which decreases the likelihood that the subject administered such treatment will manifest symptoms of the respiratory, lung or other diseases. The term "downregulate" refers to inducing a decrease in production, secretion or availability (and thus a decrease in concentration) of the targeted intracellular protein. The present invention is concerned primarily with the treatment of human subjects. However, the agents and methods disclosed here may also be employed for veterinary purposes, such as is the case in the treatment of other mammals, such as cattle, horses, wild animals, zoo animals, and domestic animals, e. g. dogs and cats. Targeted proteins may be prokaryotic or eukaryotic or mammalian and more preferably of the same species as the subject being treated. In general, "anti-sense" refers to the use of small, synthetic oligonucleotides, resembling single-stranded DNA, to inhibit gene expression by inhibiting the function of the target messenger RNA (mRNA). Milligan, J. F. et al., *J. Med. Chem.* 36(14), 1923-1937 (1993). In the present invention, inhibition of gene expression of the A<sub>1</sub> or A<sub>3</sub> adenosine receptor is desired. Gene expression is inhibited through hybridization to coding (sense) sequences in a specific messenger RNA (mRNA) target by hydrogen bonding according to Watson-Crick base pairing rules. The mechanism of anti-sense inhibition is that the exogenously applied oligonucleotides decrease the mRNA and protein levels of the target gene or cause changes in the growth characteristics or shapes of the cells. Id. See, also Helene, C. and Toulme, J., *Biochim. Biophys. Acta* 1049, 99-125 (1990); Cohen, J. S. D., Ed., *Oligodeoxynucleotides as Anti-sense Inhibitors of Gene Expression*; CRC Press: Boca Raton, FL (1987). As used herein, "anti-sense oligonucleotide" is defined as a short sequence of synthetic nucleotide that (1) hybridizes to any sense or anti-sense sequence in a mRNA or DNA which codes for the targeted protein or their double stranded counterparts, according to in vitro or in vivo hybridization conditions, described below, and (2) upon hybridization causes a decrease in gene expression of the target, e.g. adenosine or other receptor(s). The receptors discussed above are mere examples of the high power of the present technology. In fact, a large number of genes and mRNAs may be targeted in a similar manner by the present methods, to significantly down-regulate or obliterate their protein expression and observe any changes wrought to one or more functions within a system, e.g. the respiratory system and other lung disease associated targets. By means of example, in the respiratory system, the targets may be associated with difficulties of breathing, bronchoconstriction, inflammation, allergic rhinitis, chronic bronchitis, surfactant depletion, and others associated with diseases and conditions such as chronic obstructive pulmonary disease (COPD), pulmonary transplantation rejection, pulmonary infections, inhalation burns, Acute Respiratory Distress Syndrome (ARDS), cystic fibrosis, pulmonary fibrosis, radiation pneumonitis, tonsillitis, emphysema, dental pain, oral inflammation, joint pain, esophagitis, cancers afflicting the respiratory system either directly such as lung cancer, esophageal cancer, and the like, or indirectly by means of metastases, among others. These functions are of great interest because of their association with respiratory dysfunction, as is the case in asthma, allergies, allergic rhinitis, pulmonary bronchoconstriction and hypertension, chronic obstructive pulmonary disease (COPD), pulmonary transplantation rejection, pulmonary infections, allergy, asthma, cystic fibrosis (CF), Acute Respiratory Distress Syndrome (ARDS) as well as infantile and pregnancy-related RDS, cancer, etc., which either directly or by metastasis afflict the lung, the present anti-sense oligonucleotides may be directed to a list of target mRNAs, which includes the targets listed in Table 1 above, among others.

Oligonucleotides, whether DNA or RNA, may be synthesized by methods known in the art that need not be further described here. The low adenosine oligos of this invention may be obtained by first selecting fragments of a target nucleic acid having at least 4 contiguous nucleic acids selected from the group consisting of G and C and/or having a specific type and/or extent of activity, and then obtaining a first oligonucleotide 4 to 60 nucleotides long which comprises the selected fragment and has a thymidine (T) or uridine (U) nucleic acid content of up to and including about 15%, preferably, about 12%, about 10%, about 7%, about 5%, about 3%, about 1%, and more

preferably no thymidine or uridine. In one preferred embodiment, oligo(s) have a higher than natural content of Cs and Gs (orCpGs) to produce immunostimulation. The latter step may be conducted by obtaining a second oligonucleotide 4 to 60 nucleotides long comprising a sequence which is anti-sense to the selected fragment, the second oligonucleotide having an adenosine base content of up to and including about 15%, preferably about 12%, about 10%, about 7%, about 5%, about 3%, about 1%, and more preferably no adenosine. When the selected fragment comprises at least one thymidine or uridine base, an adenosine base may be substituted in the corresponding anti-sense nucleotide fragment with a universal base selected from the group consisting of heteroaromatic bases which bind to a thymidine or uridine base but have less than about 10%, preferably less than about 1%, and more preferably less than about 0.3% of the adenosine base agonist activity at the adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub> and A<sub>3</sub> receptors, and heteroaromatic bases which have no activity at the adenosine A<sub>2a</sub> receptor, when validating in the respiratory system. Other adenosine activities in other systems may be determined in other systems, as appropriate. The analogue heteroaromatic bases may be selected from all pyrimidines and purines, which may be substituted by O, halo, NH<sub>2</sub>, SH, SO, SO<sub>2</sub>, SO<sub>3</sub>, COOH and branched and fused primary and secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, arylcycloalkyl, which may be further substituted by O, halo, NH<sub>2</sub>, primary, secondary and tertiary amine, SH, SO, SO<sub>2</sub>, SO<sub>3</sub>, cycloalkyl, heterocycloalkyl and heteroaryl. The pyrimidines and purines may be substituted at all positions as is known in the art, but preferred are purines that are substituted at positions 1, 2, 3, 6 and/or 8, and pyrimidines that are substituted at 2, 3, 4, 5 and/or 6. More preferred are pyrimidines and purines such as those having the chemical formula



pyrimidines



purines

or

### PYRIMIDINES

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, and R<sup>5</sup> are independently H, alkyl, alkenyl or alkynyl and R<sup>3</sup> is H, aryl, dicycloalkyl, dicycloalkenyl, dicycloalkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, O-cycloalkyl, O-cycloalkenyl, O-cycloalkynyl, NH<sub>2</sub>-alkylamino-ketoxymethoxy-aryl, or mono or dialkylaminoalkyl-N-alkylamino-SO<sub>2</sub>aryl, and R<sup>4</sup> and R<sup>5</sup> are independently R<sup>1</sup> and together are R<sup>3</sup>, and the pyrimidines and purines optionally comprise theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline or xantine, among others. Similar modifications in the sugar are also embodiments of this invention. Reduced adenosine content of the anti-sense oligos corresponding to the thymidines (T) present in the target DNA or uridines (U) in the target RNA serves to prevent the breakdown of the oligos into products that free adenosine into the system, e.g. the lung, brain, heart, kidney, etc., tissue environment and, thereby, to prevent any unwanted effects due to it. By means of example, the NfκB transcription factor may be selected as a target, and its mRNA or DNA searched for low thymidine (T), low uridine (U) or desthymidine (desT) or desuridine (desU) fragments. Only desU and desT segments of the mRNA or DNA are selected which, in turn, will produce desA anti-sense as their complementary strand. When a number of DNA or RNA that are desT or desU segments are found, the sequence of the anti-sense segments may be deduced. Typically, about 10 to 30 and even larger numbers of desA anti-sense sequences may be obtained. These anti-sense sequences may include some or all desA anti-sense oligonucleotide sequences

corresponding to desU or desT segments of the mRNA or DNA of the target, such as anyone of those shown in Table 1 above, in Table 2 below, and others associated with functions of the brain, cardiovascular and renal systems, and many others. For each of the original desA anti-sense oligonucleotide sequences corresponding to the target gene, e.g. the NF $\kappa$ B transcription factor, typically about 10 to 30 sequences may be found within the target gene or RNA which have a low content of thymidine (DNA) or uridine (RNA). In accordance with this invention, the selected fragment sequences may also contain a small number of thymidine (DNA) or uridine (RNA) nucleotides within the secondary or tertiary or quaternary sequences. In some cases, a large adenosine content may suffice to render the anti-sense oligonucleotide less active or even inactive against the target. In accordance with this invention, these so called "non-fully desA" sequences may preferably have a content of adenosine of less than about 15%, about 12%, about 10%, about 7%, about 5%, and about 2% adenosine. Most preferred is no adenosine content (0%). In some instances, however, a higher content of adenosine is acceptable and the oligonucleotides still fail to show detrimental "adenosine activity". A particular important embodiment is that where the adenosine nucleotide is "fixed" or replaced by a "universal or alternative" base that may base-pair with similar or equal affinity to two or more of the four nucleotides present in natural DNA: A, G, C, and T.

A universal or alternative base is defined in this patent as any compound, more commonly an adenosine analogue, which has substantial capacity to hybridize to thymidine or uridine, while at the same time having reduced, or substantially lacking, ability to bind adenosine receptors or other molecules through which adenosine may exert an undesirable side effect in the experimental animal or in a cell system. Alternatively, adenosine analogs which completely fail to activate, or have significantly reduce ability for activating, adenosine receptors, such as the adenosine A<sub>1</sub>, A<sub>2b</sub> and/or A<sub>3</sub> receptors, most preferably A<sub>1</sub> receptors, and those that may even act as agonists of the adenosine A<sub>2b</sub> receptor, may be used. One example of a universal base is 2'-deoxyribofuranosyl-(5-nitroindole), and an artisan will know how to select others. This "fixing" step generates further novel sequences, different from those anti-sense to the ones found in nature, that permits the anti-sense oligonucleotide to bind, preferably equally well, with the target RNA. Other examples of universal or alternative bases are 2'-deoxyribosyl-(5-nitroindole). Other examples of universal bases are 3 - nitropyrrole - 2' - deoxynucleoside, 5 - nitro-indole, 2' - deoxyribosyl - (5 - nitroindole), 2'-deoxyribofuranosyl - (5-nitroindole), 2' - deoxyinosine, 2' -deoxynebularine, 6H, 8H-3,4-dihydropyrimido [ 4, 5 - c] oxazine - 7 - one and 2 - amino - 6 -methoxy aminopurine. In addition to the above, Universal bases which may be substituted for any other base although with somewhat reduced hybridization potential, include 3 - nitropyrrole - 2' - deoxynucleoside 2' - deoxyribofuranosyl - (5 - nitroindole), 2' - deoxyinosine and 2' - deoxynebularine (Glen Research, Sterling, VA). More specific mismatch repairs may be made using "P" nucleotide, 6H, 8H - 3, 4 - dihydropyrimido [4,5 - c] [1, 2] oxazin - 7 - one, which base pairs with either guanosine (G) or adenosine (A) and "K" nucleotide, 2 - amino - 6 - methoxyaminopurine, which base pairs with either cytidine (C) or thymidine (T)-uridine (U), among others. Others that are known in the art or will become available are also suitable. See, for example, Loakes, D. and Brown, D. M., Nucl. Acids Res. 22:4039-4043 (1994); Ohtsuka, E. et al., J. Biol. Chem.260(5):2605-2608 (1985); Lin, P.K.T. and Brown, D. M., Nucleic Acids Res. 20(19):5149-5152 (1992); Nichols, R. et al., Nature 369(6480): 492-493 (1994); Rahmon, M. S. and Humayun, N. Z., Mutation Research 377 (2): 263-8 (1997); Amosova, O., et al., Nucleic Acids Res. 25 (10): 1930-1934 (1997); Loakes D. & Brown, D. M., Nucleic Acids Res. 22 (20): 4039-4043 (1994), the entire sections relating to universal bases and their preparation and use in nucleic acid binding being incorporated herein by reference. When non-fully desT sequences are found in the naturally occurring target, they typically are selected so that about 1 to 3 universal base substitutions will suffice to obtain a 100% "desA" anti-sense oligonucleotide. Thus, the present method provides either anti-sense oligonucleotides to different targets which are low in, or devoid of, A content, as well as anti-sense oligonucleotides where one or more adenosine nucleotides, e. g. about 1 to 3, or more, may be "fixed" by replacement with a "universal" or "replacement" base. Universal bases are known in the art and need not be listed herein. An artisan will know which bases may act as universal bases, and replace them for A. Table 2 below provides a selected number of targets to which the agents of the invention are effectively applied. Others, however, may also be targeted.

**Table 2: Cancer Targets**

Transforming Oncogenes	Therapy Targets
ras	thymidylate synthetase
src	thymidylate synthetase



	myc	dihydrofolate reductase
	bcl-2	thymidine kinase
		deoxycytidine kinase
		ribonucleotide reductase
5	Angiogenesis factors	Adhesion Molecules
	Oncogenes	Folate Pathway Enzymes
	DNA repair genes	(One Carbon Pool)
		Telomerase
		HMG CoA Reductase
10		Farnesyl Transferase
		Glucose-6-Phosphate Transferase Akt2 (Bases 1-1715)
	Akt3 (1-1547)	
	Ampiregulin (1-1230))	
	Ap-2 (1-1391)	
15	Ap-2 Beta	
	Ap-2 Gamma	
	Sphingomyelinase	
	Beta-2-Adrenergic Receptor	
	Beta Catenin	
20	E2F-Related Transcription Factor	
	HM bFGF	
	B-cell translocation gene 1 (BTG1)	
	cyclin-dependent kinase 2 (CDK2)	
	cyclin-dependent kinase 2 (CDK2)	
25	cyclin-dependent kinase 3 (CDK3)	
	cyclin-dependent kinase 4 (CDK4)	
	cyclin-dependent kinase 5 (CDK5)	
	c-ets-1 proto-oncogene	
	checkpoint kinase Chk1 (CHK1)	
30	type IV collagenase	
	hepatocyte growth factor receptor (c-met)	
	<u>MYB proto-oncogene protein (MYB)</u>	

A group of preferred targets for the treatment of cancer are genes associated with any of different types of cancers, or those generally known to be associated with malignancies, whether they are regulatory or involved in the production of RNA and/or proteins. Examples are transforming oncogenes, including, but not limited to, ras, src, myc, and BCL-2, among others. Other targets are those to which present cancer chemotherapeutic agents are directed to, such as various enzymes, primarily, although not exclusively, thymidylate synthetase, dihydrofolate reductase, thymidine kinase, deoxycytidine kinase, ribonucleotide reductase, and the like. The present technology is particularly useful in the treatment of cancer ailments given that traditional cancer therapies are fraught with the unresolved problem of selectively killing cancer cells while preserving normal living cells from the devastating effects of treatments such as chemotherapy, radiotherapy, and the like. The present technology provides the ability of selectively attenuating or enhancing a desired pathway or target. This approach provides a significant advantage over standard treatments of cancer because it permits the selection of a pathway, including primary, secondary and possibly tertiary targets, which are not generally expressed simultaneously in normal cells. Thus, the present agent may be administered to a subject to cause a selective increase in toxicity within tumor cells that, for instance, express all three targets while normal cells that may express only one or two of the targets will be significantly less affected or even spared. A group of preferred targets for the treatment of cancers are genes associated with different types of cancers, or those generally known to be associated with malignancies, whether they are regulatory or involved in the production of RNA and/or proteins. Examples are transforming oncogenes, including, but not limited to, ras, src, myc, and BCL-2, among others. Other targets are those to which present cancer chemotherapeutic agents are directed to, such as various enzymes, primarily, although not exclusively, thymidylate synthetase, dihydrofolate

reductase, thymidine kinase, deoxycytidine kinase, ribonucleotide reductase, and the like.

In one embodiment, at least one of the genes or mRNAs to which the oligo of the invention is targeted encodes or is involved in the regulation of a protein such as transcription factors, stimulating and activating factors, intracellular and extracellular receptors and peptide transmitters in general, interleukins, interleukin receptors, chemokines, chemokine receptors, endogenously produced specific and non-specific enzymes, immunoglobulins, antibody receptors, central nervous system (CNS) and peripheral nervous and non-nervous system receptors, CNS and peripheral nervous and non-nervous system peptide transmitters, adhesion molecules, defensins, growth factors, vasoactive peptides and receptors, and binding proteins, among others; or the mRNA is corresponding to an oncogene and other genes associated with various diseases or conditions. Examples of target-proteins are eotaxin, major basic protein, preproendothelin, eosinophil cationic protein, P-selectin, STAT 4, MIP-1 $\alpha$ , MCP-2, MCP-3, MCP-4, STAT 6, c-mas, NF-IL-6, cyclophilins, PDG2, cyclosporin A-binding protein, FK5-binding protein, fibronectin, LFA-1 (CD11a/CD18), PECAM-1, C3bi, PSGL-1, CD-34, substance P, p150,95, Mac-1 (CD11b/CD18), VLA-4, CD-18/CD11a, CD11b/CD18, C5a, CCR1, CCR2, CCR4, CCR5, and LTB-4, among others. Others are, however, suitable, as well. In another embodiment, at least one of the mRNAs to which the oligo is targeted encodes intracellular and extracellular receptors and peptide transmitters such as sympathomimetic receptors, parasympathetic receptors, GABA receptors, adenosine receptors, bradykinin receptors, insulin receptors, glucagon receptors, prostaglandin receptors, thyroid receptors, androgen receptors, anabolic receptors, estrogen receptors, progesterone receptors, receptors associated with the coagulation cascade, adenohipophyseal receptors, adenohipophyseal peptide transmitters, and histamine receptors (HisR), among others. However others are also contemplated. The encoded sympathomimetic receptors and parasympathomimetic receptors include acetylcholinesterase receptors (AcChaseR) acetylcholine receptors (AcChR), atropine receptors, muscarinic receptors, epinephrine receptors (EpiR), dopamine receptors (DOPAR), and norepinephrine receptors (NEpiR), among others. Further examples of encoded receptors are adenosine A<sub>1</sub> receptor, adenosine A<sub>2b</sub> receptor, adenosine A<sub>3</sub> receptor, endothelin receptor A, endothelin receptor B, IgE high affinity receptor, muscarinic acetylcholine receptors, substance P receptor, histamine receptor, CCR-1 CC chemokine receptor, CCR-2 CC chemokine receptor, CCR-3 CC chemokine receptor (Eotaxin Receptor), interleukin-1 $\beta$  receptor (IL-1 $\beta$ R), interleukin-1 receptor (IL-1R), interleukin-1 $\beta$  receptor (IL-1 $\beta$ R), interleukin-3 receptor (IL-3R), CCR-4 CC chemokine receptor, cysteinyl leukotriene receptors, prostanoid receptors, GATA-3 transcription factor receptor, interleukin-1 receptor (IL-1R), interleukin-4 receptor (IL-4R), interleukin-5 receptor (IL-5R), interleukin-8 receptor (IL-8R), interleukin-9 receptor (IL-9R), interleukin-11 receptor (IL-11R), sympathomimetic receptors, parasympathomimetic receptors, GABA receptors, adenosine receptors, bradykinin receptors, e.g. bradykinin B2 receptor, insulin receptors, glucagon receptors, prostaglandin receptors, thyroid receptors, androgen receptors, anabolic receptors, estrogen receptors, progesterone receptors, receptors associated with the coagulation cascade, adenohipophyseal receptors, and histamine receptors (HisR). Others are also contemplated even though not listed herein. The encoded enzymes for development of the oligos of the invention include synthetases, kinases, oxidases, phosphatases, reductases, polysaccharide, triglyceride, and protein hydrolases, esterases, elastases, and , polysaccharide, triglyceride, lipid, and protein synthases, among others. Examples of target enzymes are tryptase, inducible nitric oxide synthase, cyclooxygenase (Cox), MAP kinase, eosinophil peroxidase,  $\beta$ 2-adrenergic receptor kinase, leukotriene c-4 synthase, 5-lipoxygenase, phosphodiesterase IV, metalloproteinase, tryptase, CSBP/p38 MAP kinase, neutrophil elastase, phospholipase A<sub>2</sub>, cyclooxygenase 2 (Cox-2), fucosyl transferase, chymase, protein kinase C, thymidylate synthetase, dihydrofolate reductase, thymidine kinase, deoxycytidine kinase, and ribonucleotide reductase, among others. Any enzyme associated with a disease or condition, however, is suitable as a target for this invention. Suitable encoded factors for application of this invention are, among others, Nf $\kappa$ B transcription factor, granulocyte macrophage colony stimulating factor (GM-CSF), AP-1 transcription factor, GATA-3 transcription factor, monocyte activating factor, neutrophil chemotactic factor, granulocyte/macrophage colony-stimulating-factor (G-CSF), NFAT transcription factors, platelet activating factor, tumor necrosis factor  $\alpha$  (TNF  $\alpha$ ), and basic fibroblast growth factor (BFGF). Additional factors are also within the invention even though not specifically mentioned. Suitable adhesion molecules for use with this invention include intracellular adhesion molecules 1 (ICAM-1), 2 (ICAM-2) and 3 (ICAM-3), vascular cellular adhesion molecule (VCAM), endothelial leukocyte adhesion molecule-1 (ELAM-1), neutrophil adherence receptor, mad CAM-1, and the like. Other known and unknown factors (at this time) may also be targeted herein. Among the cytokines, lymphokines and chemokines preferred are interleukin-1 (IL-1), interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-3 (IL-3), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-8 (IL-8),

interleukin-9 (IL-9), interleukin-11 (IL-11), CCR-5 CC chemokine, and Rantes. Other examples include H2A histone family, member N, Tubulin, beta polypeptide, ELL gene (11-19 lysine-rich leukemia gene) 7-dehydrocholesterol reductase, ADP-ribosylation factor-like 7, Karyopherin alpha 2 (RAG cohort 1, importin alpha 1), EST (AI038433), EST (AI122689), EST (AI092623), ESTs (AI095492), ESTs (AI138216), ESTs (AI128305), ESTs (AI125228), ESTs (AI041482), ESTs (AI051839), Homo sapiens mRNA; cDNA DKFZp434A1716, ESTs (AI096522), ESTs (AI122807), ESTs (AI041212), EST (AI125651), Enolase 1, (alpha), EST (AI024215), EST (AI034360), Homo sapiens mRNA; cDNA DKFZp564H0764, Homo sapiens mRNA for KIAA1363 protein, partial cds, Potassium voltage-gated channel, shaker-related subfamily, beta member 2, ER-associated DNAJ; ER-associated Hsp40 co-chaperone; hDj9; ERj3, ESTs, Weakly similar to p38 protein [H.sapiens] (AA906703), CGI-142, ESTs (AA463249), Homo sapiens clone 25058 mRNA sequence ESTs (R49144), Squamous cell carcinoma antigen 1, ESTs (AA425700), Myosin X, ESTs (AA459692), Epithelial protein lost in neoplasm beta, CD44 antigen (homing function and Indian blood group system), Coagulation factor III (thromboplastin, tissue factor), ESTs (AA909635), Adducin 1 (alpha), 5' Nucleotidase (CD73), ESTs, Moderately similar to semaphorin C [M.musculus] (AA293300), ESTs (AA278764), ESTs (AA678160), Calmodulin 2 (phosphorylase kinase, delta), ESTs (R42770), Chloride intracellular channel 1, High-mobility group (nonhistone chromosomal) protein 17, Ubiquitin carrier protein, Tubulin, alpha 1 (testis specific), Transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase), Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican), Proteasome (prosome, macropain) 26S subunit, non-ATPase, 2, Tubulin, beta polypeptide, Filamin B, beta (actin-binding protein-278), Stanniocalcin, Low density lipoprotein receptor (familial hypercholesterolemia), Plectin 1, intermediate filament binding protein, 500kD, S100 calcium-binding protein A2, Immediate early response 3, Calpain, large polypeptide L2, Pleckstrin homology-like domain, family A, member 1, Melanoma adhesion molecule, CD44 antigen (homing function and Indian blood group system), Programmed cell death 5, Hexokinase 1, Vascular endothelial growth factor, Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor), Calumenin, Syntaxin 11, Diphtheria toxin receptor (heparin-binding epidermal growth factor-like growth factor), Fn14 for type I transmembrane protein, Nef-associated factor 1, High-mobility group (nonhistone chromosomal) protein isoforms I and Y, Catechol-O-methyltransferase, C-terminal binding protein 1, Collagen, type XVII, alpha 1, ESTs (N58473), Farnesyl-diphosphate farnesyltransferase 1 RNA helicase-related protein, Interferon stimulated gene (20kD), Steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1), Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase), Laminin, alpha 3 (nicein (150kD), kalinin (165kD), BM600 (150kD), epilegrin), Collagen, type XVII, alpha 1, Keratin 18, Heparan sulfate (glucosamine) 3-O-sulfotransferase 1, Tubulin, alpha 2, Adenylyl cyclase-associated protein, Forkhead box D1, Cathepsin C, ESTs, Highly similar to AF151802\_1 CGI-44 protein [H.sapiens] (T74688), Ribonucleotide reductase M2 polypeptide, Laminin, gamma 2 (nicein (100kD), kalinin (105kD), BM600 (100kD), Herlitz junctional epidermolysis bullosa)), Homo sapiens mRNA; cDNA DKFZp586P1622 (from clone DKFZp586P1622), ESTs, Weakly similar to /prediction (AA284245), and Lactate dehydrogenase A. Others, however, may also be targeted, as they are known to be involved in specific diseases or conditions to be treated, or for their generic activities, such as inflammation. Examples of defensins for the practice of this invention are defensin 1, defensin 2, and defensin 3, and of selectins are  $\alpha 4\beta 1$  selectin,  $\alpha 4\beta 7$  selectin, LFA-1 selectin, E-selectin, P-selectin, and L-selectin. Examples of oncogenes, although not an all inclusive list, are ras, src, myc, and bcBCL. Others, however, are also suitable for use with this invention.

The agents administered in accordance with this invention are preferably designed to be anti-sense to one or more target genes and/or mRNAs usually related in origin to the species to which it is to be administered, although they may be directed, to foreign sequences, e.g. of viruses. When treating humans, the agents are preferably designed to be anti-sense to a human gene or RNA. The agents of the invention encompass oligonucleotides which are anti-sense to naturally occurring DNA and/or RNA sequences, fragments thereof of up to a length of one (1) base less than the targeted sequence, preferably at least about 7 nucleotides long, oligos having only over about 0.02%, more preferably over about 0.1%, still more preferably over about 1%, and even more preferably over about 4% adenosine nucleotides, and up to about 30%, more preferably up to about 15%, still more preferably up to about 10% and even more preferably up to about 5%, adenosine nucleotide, or lacking adenosine altogether, and oligos in which one or more of the adenosine nucleotides have been replaced with so-called universal bases, which may pair up with thymidine or uridine nucleotides but fail to substantially trigger adenosine receptor activity. Examples of human sequences and fragments, which are not limiting, of anti-sense oligonucleotide of the

Some of the examples of anti-sense oligonucleotide sequence fragments target the initiation codon of the respective gene, and in some cases adenosine is substituted with a universal or alternative base adenosine analogue denoted as “B”, which lacks ability to bind to the adenosine A<sub>1</sub> and/or A<sub>3</sub> receptors. In fact, such replacement nucleotide acts as a “spacer”. Many of the examples shown below provide one such sequence and many fragments overlapping the initiation codon, preferably wherein the number of nucleotides n is about 7, about 10, about 12, about 15, about 18, about 21 and up to about 28, about 35, about 40, about 50, about 60.

## Human Receptor-related Antisense Polynucleotide

36

GTGTCTTTCC TTTGCTCTTG GTGTGTCTTT GCTGTGCCCT GCCTCTCTGC GGGGGTGGCT TCCTGCCGCG TCTCTGGGCC  
 GTCCCGTCCC TCGGCCCGCG GCCGCGCTCG GCTCCTCTCC CTCTGGCCCG GCTCGGGGCG GGGCGGGGCG GTGGGCGGGC  
 GGCCTGCCCC TCGCGCGCGG GCTGGCCCCCT GCTGGCCGTC GGCTGCGCGC TGCTGGCTGC CCTGCTGGCC GCGCCCGGGC  
 CTGTCCGCGT TCGCGCGCGC TGCTCTCTTG CTGTCTCTTG GCTGGGTGGG CTGGGCGCGC CTGGCCCGGTG  
 5 CTGGGGCTCC TCGGGGGGGG GGGCTCTTCC GGGCTGTCTC CCTCCGGGGC GGGGGTTTCT GGCCGTGGGG GTCTTGCCCTG  
 GCCTCCGGGC TCCTGCTTGT CTGCTCTCC TTCTCTGGTC GGTGTGGCT CGGGGCTCCG TGGGTCCCTG GCGCCCGTTT  
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 CCTGCTGCTC TTGGTTTGG GCTTTTTC TCTCTCTCT TTTCTGTGCG TGGGCTCC GCACGCTCT TGCCACCTCC  
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5 **Human Enzyme-related Antisense Polynucleotide**  
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**Human Factor Related Anti-sense Oligonucleotide**

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 TCTGAGTCCG CTGGAGCGGG CTTGGGCAGC CAACGGCAGC ATGGGGGAGC CCGTGATCAA GTGCGAGGTTT GAGGAAGTCA  
 5 TCAGCATGGA GTACATGGTC TACTTCAACT TCTTTGTGTG GGTGCTGCCC CCGCTTCTCC TCATGGTCTCT CATCTACCTG  
 GAGGTCTTCT ACCTAATCCG CAAGCAGCTC AACAAGAAGG TGTCCGGCCTC CTCCGGCGAC CCGCAGAAAGT ACTATGGGAA  
 GGAGCTGAAG ATCGCCAAAGT CGCTGGCCCT CATCCTCTTC CTCTTTGCCC TCAGCTGGGT GCCTTTGCAC ATCCTCAACT  
 GCATACCCCT CTCTGCCCT TCCTGCCACA AGCCAGCAT CTCTACCTAC ATTGCCATCT TCCTCACGCA CGGCAACTCG  
 10 GCCATGAACC CCATTGTCTA TGCCCTCCGC ATCCAGAAAT TCCGCTACAC CTTCCTTAAG ATTTGGAATG ACCATTTCGG  
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 GTTGGCTGGG GGCATGGGGG AGGCTCTGAA GAGATACCCA CAGAGTGTGG TCCCTCCACT AGGAGTTAAT TACCCTAGAC  
 CTCTGGGCCC TGCAGGAGGC CTGGGAGGGC AAGGGTCTTA CGAGGGGACC AGGTGTCTAG AGGCAACAGT GTTCTGAGCC  
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 15 CCACCTGGGC TGGGAGAAGG TGCTTGGGCT TCTGCGGTGA GGCAGGGGAG TCTGCTTGT TTAGATGTTG GTGCTGCAGC  
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 TCTGTAGGAG AGACTGGCCA GA -3' (FRAG. NO: 11803)  
 5'- ATGAGTGTCA GAAGTGTGAA GGGTGCCTGT TCTGAATCCC AGAGCCTCCT CTCCCTCTGT GAGGCTGGCA GGTGAGGAAG  
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 20 TCAGGCAGCC GGGAGCTCTG CCAGCTTTGG TGACCTTGGG CCGGGCTGGG AGCGCTGCGG CGGGAGCCGG AGGACTATGA  
 GCTGCCGCGG GTTGTCCAGA GCCCAGCCCA GCCCTACGCG CGCGGCCCGG AGCTCTGTTT CTGTGAACTT TGGCAACTGC  
 CTCTGGGACC CTTGCCGGCC AGCAGGCAGG ATGGTGTCTG CCTCGTGCCC CTGTGTGCCC GTCTGTGAT GTGCCAGCC  
 TGTGCCCGCC ATGCCGCCCT CCATCTCAGC TTTCAGGCC GCCTACATCG GCATCGAGGT GCTCATCGCC CTGGTCTCTG  
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 25 CTGGCGGTGC CTGATGTGGC CGTGGGTGCC CTGTATCCTC CCTCGCCAT CCTCATCAAC ATTTGGCCAC AGACCTACTT  
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 TGCTGGATCC TCTCCTCTGT GGTGGGACTG ACCCCTATGT TTGGCTGGAA CAATCTGAGT GCGGTGGAGC GGGCCTGGGC  
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 30 ACTTCTTGT GTGGGTGCTG CCCCCTCTC TCTCATGTT CTGAGGTCT TCTGAGGTCT TCTACTAAT CCGCAAGCAG  
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 35 GGATCTCCCA GAAGAGAGGC CTGATGACTA GACCCCGCCT TCCGCTCCCA CCAGCCACA TCCAGTGGG TCTCAGTCCA  
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 50 CCTGTCTGTC ATGTGAATCC CTCAATACCC CTAGTATCTG GCTGGGTTT CAGGGGCTT GGAAGCTCTG TTGCAAGGTG  
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 GGGGGCAAGT TGGGGGAGCC TGGAGCCCTT TGTGGGAGG GTGAGCCGGG GAGCCCTGGA CCCCCTGTGT GGGAGGCGCA  
 GCGGGGGGAT CCTGGAGCCC CTGTGTCGGG GGGCGAGGGA GGGGAGGTGG CCGTCCGTTG ACCTTCTGAA CATGAGTGT  
 AACTCCAGGA CTGTCTTCCA AGCCCTTCCC TCTGTTGAA ATTGGGTGTG CCCTGGCTCC CAAGGGAGGC CCATGTGACT  
 AATAAAAAAC TGTGAACCTT -3' (FRAG. NO: 11802)  
 5'- ATGCCGCCCT CCATCTCAGC TTTCCAGGCC CCCTACATCG GCATCGAGGT GCTCATCGCC CTGGTCTCTG TGCCCGGGAA  
 55 CGTGTGGTG ATCTGGGCGG TGAAGGTGAA CCAGGCGCTG CCGGATGCCA CCTTCTGCTT CATCGTCTCG CTGGCGGTGG  
 CTGATGTGGC CGTGGGTGCC CTGGTCATCC CCCTCGCCAT CCTCATCAAC ATTTGGCCAC AGACCTACTT CCACACCTGC  
 CTCATGGTTG CTTGTCCGGT CCTCATCTC ACCCAGAGCT CCATCCTGGC CCGTCTGGCA ATTTGTGTGG ACCGCTACCT  
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 60 TCTCCTCTGT GGTGGGACTG ACCCCTATGT TTGGCTGGAA CAATCTGAGT GCGGTGGAGC GGGCCTGGGC AGCCAACGGC  
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 GTGGGTGCTG CCCCCTCTC TCCTCATGTT CCTCATCTAC CTGGAGGTCT TCTACTAAT CCGCAAGCAG CTCAACAAGA  
 AGGTGTGGC CTCTCCGGG GACCCGAGA AGTACTATGG GAAGGAGCTG AAGATCGCCA AGTCGCTGGC CCTCATCTC  
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 65 CATCCTTACC TACATTGCCA TCTTCTCAC GCACGGCAAC TCGGCCATGA ACCCAATTG CTATGCTTCT CGCATCCAGA  
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 GAAGAGAGGC CTGATGACTA G-3' (FRAG. NO: 11801)  
 5'-CCGATTTGTG TTTTAATAAA AGAATCTGGA AGATAAATAG TCTTGAAGAG AGACAAAGGA AGGAAAATTT AAATCCTTAG  
 70 ATTCAAGCAG AAGAATTCCA TGTGGAAGGT TTGGGTGTT GTTGTGTTG TTTGGTGTG TTTTGTGTTT TTTGTTTTT  
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 CATCCCTCTG GAGCTTACC GCGGGCCTTG GCTTCCCCAG GAATCCCTGG AGCTAGCGG TGCTGAAGGC GTCCGAGGTG  
 GGGGGCACTT GGACAGAACA GTCAGGCAGC CCGGAGCTCT GCGAGCTTTG GTGACCTTGG GTGCTTGGCT CTGAGCCCTT  
 GGTGCCCGTC TGCTGATGTG CCCAGCCTGT GCGCGCCATG CCGCCCTCCA TCTCAGCTTT CCAGGCCGCC TACATCGGCA  
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 75 GATGCCACCT TCTGCTTCA CGTGTGCTG CCGGTGGCTG ATGTGGCCGT GGGTGCCCTG GTCATCCCC TCGCCATCCT

CATCAACATT GGGCCACAGA CCTACTTCCA CACCTGCCTC ATGGTTGCCT GTCCGGTCCT CATCCTCACC CAGAGCTCCA  
 TCCTGGCCCT GCTGGCAATT GCTGTGGACC GCTACCTCCG GGTCAAGATC CCTCTCCGGT ACAAGATGGT GGTGACCCCC  
 CGGAGGGCGG CGGTGGCCAT AGCCGGCTGC TGGATCCTCT CTTCTCGTGT GGGACTGACC CCTATGTTTG GCTGGAACAA  
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 5 TCAGCATGGA GTACATGGTC TACTTCAACT TCTTTGTGTG GGTGTGCCC CCGCTTCTCC TCATGGTCTT CATCTACCTG  
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 10 GCCATGAACC CCAITGTCTA TGCTTCCGC ATCCAGAAAGT TCCGCGTCAC CTCTCTTAAG ATTTGGAATG ACCATTTCGG  
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 15 CCACCTGGGC TGGGAGAAAG TGCTTGGGCT TCTGCGGTGA GGCAGGGGAG TCTGCTGTG TTAGATGTTG GTGGTGCAGC  
 CCCAGGACCA AGCTTAAGGA GAGGAGAGCA TCTGCTCTGA GACGGATGGA AGGAGAGAGG TTGAGGATGC ACTGGCCTGT  
 TCTGTAGGAG AGACTGGCCA GA -3'  
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 TCAGGCAGCC GGGAGCTCTG CCAGCTTTGG TGACCTTGG CCGGCTGGG AGCGCTGCGG CGGGAGCCGG AGGACTATGA  
 GCTGCCGCGC GTTGTCCAGA GCCCAGCCCA GCCCTACGCG CGCGGCCCGG AGCTCTGTTC CCTGGAACCT TGGGCACTGC  
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 25 TGCCCGGAA CGTGTGGTG ATCTGGGCGG ATCTGGGCGG CAAGGCGCTG CGGGATGCCA CCTTCTGTCT GTGCTGTCTG  
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 30 AGCCAAACGG AGCATGGGG AGCCCGTGAT CAAGTGCAG TCTGAGAAGG TCATCAGCAT GGAGTACATG GTCTACTTCA  
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 CCTCATCTC TTCTCTTTG CCCTCAGCTG GCTGCCCTTG CATACCTCA ACTGCATCAC CCTCTTCTG CCGTCTGCTC  
 ACAAGCCAG CATCTTACC TACATTGCCA TCTTCTCAC CACCGGCAAC TCGGCCATGA ACCCATTTGT CTATGCCCTT  
 35 CGCATCCAGA AGTTCGCGT CACCTTCTT AAGATTTGGA ATGACCATTT CCGCTGCCAG CCTGCACCTC CCATTGACGA  
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 40 GGGCAAGGGT CCTACGGAG GACCAGGTGT CTAGAGGCAA CAGTGTCTG AGCCCCACC TGCCTGACCA TCCCATGAGC  
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 50 CTTGTGCTG ATGTGAATCC CTCAATACCC CTAGATCTG CTGTGGTGT CAGGGGCTTT CAGGGGCTTT TTGCAGGTGT  
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 GCGGGGGGAT CCTGGAGCCC CTGTGTCCGG TGGCGAGGGA GGGGAGGTGG CCGTCCGTTG ACCTTCTGAA CATGAGTGTG  
 AACTCCAGGA CTTGCTTCCA AGCCCTTCCC TCTGTGGAA ATGGGTGTG CCCTGGCTCC CAAGGAGGC CCATGTGACT  
 55 AATAAAAAAC TGTGAACCT -3' (FRAG. NO: ) (SEQ ID NO:11790)  
 5'-ATGCCGCCCT CCATCTCAGC TTTCCAGGCC GCCTACATCG GCATCGAGGT GCTCATCGCC CTGGTCTCTG TGCCCGGGA  
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 CTGATGTGGC CGTGGGTGCC CTGGTCATCC CCTCGCCAT CCTCATCAAC ATTTGGGCCAC AGACCTACTT CCACACCTGC  
 CTCATGGTGG CCTGTCCGTT CCTATCCTC ACCCAGAGCT CCATCCTGGC CTGTCTGGCA ATTGCTGTGG ACCGCTACCT  
 60 CCGGGTCAAG ATCCCTCTCC GGTACAAGAT GGTGGTGACC CCGCGGAGGG CCGCGGTGGC CATAGCCGGC TGCTGGATCC  
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 65 TTCTCTTTG CCTCAGCTG GCTGCCCTTG CACATCTCA ACTGCATCAC CCTCTTCTG CCGTCTGCC ACAAGCCAG  
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 GAAGAGAGGC CTGATGACTA G (FRAG. NO: ) (SEQ ID NO:12483)  
 5'-GAT GGA GGG CGG CAT GGC GGG-3' (FRAG. NO: 1657) (SEQ ID NO:11781)  
 70 5'-G CGG GTC GCC GG-3' (FRAG. NO: 1658) (SEQ ID NO:11782)  
 5'-GGC GGC CBC BGG C-3' (FRAG. NO: 1659) (SEQ ID NO:11783)  
 5'-GGC GGC CBC-3' (FRAG. NO: 1660) (SEQ ID NO:11784)  
 5'-GC GGC CTG G-3' (FRAG. NO: 1661) (SEQ ID NO:11785)  
 5'-GGB GGG CGG C-3' (FRAG. NO: 1662) (SEQ ID NO:11786)  
 75 5'-GBT GGB GGG-3' (FRAG. NO: 1663) (SEQ ID NO:11787)



[illegible]



5'-GGC GGC CTG GAA AGC TGA G-3' (FRAG 75) (SEQ ID NO:9454)  
5'-GGC GGC CTG GAA AGC TGA-3' (FRAG 76) (SEQ ID NO:9455)  
5'-GGC GGC CTG GAA AGC TG-3' (FRAG 77) (SEQ ID NO:9456)  
5'-GGC GGC CTG GAA AGC T-3' (FRAG 78) (SEQ ID NO:9457)  
5 5'-GGC GGC CTG GAA AGC-3' (FRAG 79) (SEQ ID NO:9458)  
5'-GGC GGC CTG GAA AG-3' (FRAG 80) (SEQ ID NO:9459)  
5'-GGC GGC CTG GAA A-3' (FRAG 81) (SEQ ID NO:9460)  
5'-GGC GGC CTG GAA-3' (FRAG 82) (SEQ ID NO:9461)  
5'-GGC GGC CTG GA-3' (FRAG 83) (SEQ ID NO:9462)  
10 5'-GGC GGC CTG G-3' (FRAG 84) (SEQ ID NO:9463)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 85) (SEQ ID NO:9464)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 86) (SEQ ID NO:9465)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 87) (SEQ ID NO:9466)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG-3' (FRAG 88) (SEQ ID NO:9467)  
15 5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 89) (SEQ ID NO:9468)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 90) (SEQ ID NO:9469)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG-3' (FRAG 91) (SEQ ID NO:9470)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 92) (SEQ ID NO:9471)  
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20 5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 94) (SEQ ID NO:9473)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 95) (SEQ ID NO:9474)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 96) (SEQ ID NO:9475)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG-3' (FRAG 97) (SEQ ID NO:9476)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG-3' (FRAG 98) (SEQ ID NO:9477)  
25 5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 99) (SEQ ID NO:9478)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC-3' (FRAG 100) (SEQ ID NO:9479)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GG-3' (FRAG 101) (SEQ ID NO:9480)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT G-3' (FRAG 102) (SEQ ID NO:9481)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT-3' (FRAG 103) (SEQ ID NO:9482)  
30 5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 104) (SEQ ID NO:9483)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG C-3' (FRAG 105) (SEQ ID NO:9484)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CGG-3' (FRAG 106) (SEQ ID NO:9485)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG CG-3' (FRAG 107) (SEQ ID NO:9486)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GGG C-3' (FRAG 108) (SEQ ID NO:9487)  
35 5'-GC GGC CTG GAA AGC TGA GAT GGA GGG-3' (FRAG 109) (SEQ ID NO:9488)  
5'-GC GGC CTG GAA AGC TGA GAT GGA GG-3' (FRAG 110) (SEQ ID NO:9489)  
5'-GC GGC CTG GAA AGC TGA GAT GGA G-3' (FRAG 111) (SEQ ID NO:9490)  
5'-GC GGC CTG GAA AGC TGA GAT GGA-3' (FRAG 112) (SEQ ID NO:9491)  
5'-GC GGC CTG GAA AGC TGA GAT GG-3' (FRAG 113) (SEQ ID NO:9492)  
40 5'-GC GGC CTG GAA AGC TGA GAT G-3' (FRAG 114) (SEQ ID NO:9493)  
5'-GC GGC CTG GAA AGC TGA GAT-3' (FRAG 115) (SEQ ID NO:9494)  
5'-GC GGC CTG GAA AGC TGA GA-3' (FRAG 116) (SEQ ID NO:9495)  
5'-GC GGC CTG GAA AGC TGA G-3' (FRAG 117) (SEQ ID NO:9496)  
5'-GC GGC CTG GAA AGC TGA-3' (FRAG 118) (SEQ ID NO:9497)  
45 5'-GC GGC CTG GAA AGC TG-3' (FRAG 119) (SEQ ID NO:9498)  
5'-GC GGC CTG GAA AGC T-3' (FRAG 120) (SEQ ID NO:9499)  
5'-GC GGC CTG GAA AGC-3' (FRAG 121) (SEQ ID NO:9500)  
5'-GC GGC CTG GAA AG-3' (FRAG 122) (SEQ ID NO:9501)  
5'-GC GGC CTG GAA A-3' (FRAG 123) (SEQ ID NO:9502)  
50 5'-GC GGC CTG GAA-3' (FRAG 124) (SEQ ID NO:9503)  
5'-GC GGC CTG GA-3' (FRAG 125) (SEQ ID NO:9504)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 126) (SEQ ID NO:9505)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 127) (SEQ ID NO:9506)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 128) (SEQ ID NO:9507)  
55 5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG-3' (FRAG 129) (SEQ ID NO:9508)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 130) (SEQ ID NO:9509)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 131) (SEQ ID NO:9510)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG-3' (FRAG 132) (SEQ ID NO:9511)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 133) (SEQ ID NO:9512)  
60 5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT TGC GGG CAC A-3' (FRAG 134) (SEQ ID NO:9513)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 135) (SEQ ID NO:9514)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT TGC GGG CA-3' (FRAG 136) (SEQ ID NO:9515)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT TGC GGG C-3' (FRAG 137) (SEQ ID NO:9516)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT TGC GGG-3' (FRAG 138) (SEQ ID NO:9517)  
65 5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT TGC GG-3' (FRAG 139) (SEQ ID NO:9518)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT TGC G-3' (FRAG 140) (SEQ ID NO:9519)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT TGC-3' (FRAG 141) (SEQ ID NO:9520)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GG-3' (FRAG 142) (SEQ ID NO:9521)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT G-3' (FRA 143) (SEQ ID NO:9522)  
70 5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT-3' (FRAG 144) (SEQ ID NO:9523)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 145) (SEQ ID NO:9524)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG C-3' (FRAG 146) (SEQ ID NO:9525)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CGG-3' (FRAG 147) (SEQ ID NO:9526)  
5'-C GGC CTG GAA AGC TGA GAT GGA GGG CG-3' (FRAG 148) (SEQ ID NO:9527)  
75 5'-C GGC CTG GAA AGC TGA GAT GGA GGG C-3' (FRAG 148) (SEQ ID NO:9528)

- 5'-C GGC CTG GAA AGC TGA GAT GGA GGG -3' (FRAG 150) (SEQ ID NO:9529)  
 5'-C GGC CTG GAA AGC TGA GAT GGA GG -3' (FRAG 151) (SEQ ID NO:9530)  
 5'-C GGC CTG GAA AGC TGA GAT GGA G -3' (FRAG 152) (SEQ ID NO:9531)  
 5'-C GGC CTG GAA AGC TGA GAT GGA -3' (FRAG 153) (SEQ ID NO:9532)  
 5 5'-C GGC CTG GAA AGC TGA GAT GG -3' (FRAG 154) (SEQ ID NO:9533)  
 5'-C GGC CTG GAA AGC TGA GAT G -3' (FRAG 155) (SEQ ID NO:9534)  
 5'-C GGC CTG GAA AGC TGA GAT -3' (FRAG 156) (SEQ ID NO:9535)  
 5'-C GGC CTG GAA AGC TGA GA-3' (FRAG 157) (SEQ ID NO:9536)  
 5'-C GGC CTG GAA AGC TGA G-3' (FRAG 158) (SEQ ID NO:9537)  
 10 5'-C GGC CTG GAA AGC TGA-3' (FRAG 159) (SEQ ID NO:9538)  
 5'-C GGC CTG GAA AGC TG-3' (FRAG 160) (SEQ ID NO:9539)  
 5'-C GGC CTG GAA AGC T-3' (FRAG 161) (SEQ ID NO:9540)  
 5'-C GGC CTG GAA AGC-3' (FRAG 162) (SEQ ID NO:9541)  
 5'-C GGC CTG GAA AG-3' (FRAG 163) (SEQ ID NO:9542)  
 15 5'-C GGC CTG GAA A-3' (FRAG 164) (SEQ ID NO:9543)  
 5'-C GGC CTG GAA-3' (FRAG 165) (SEQ ID NO:9544)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 166) (SEQ ID NO:9545)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 167) (SEQ ID NO:9546)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 168) (SEQ ID NO:9547)  
 20 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 169) (SEQ ID NO:9548)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 170) (SEQ ID NO:9549)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 171) (SEQ ID NO:9550)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 172) (SEQ ID NO:9551)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 173) (SEQ ID NO:9552)  
 25 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 174) (SEQ ID NO:9553)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 175) (SEQ ID NO:9554)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 176) (SEQ ID NO:9555)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 177) (SEQ ID NO:9556)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 178) (SEQ ID NO:9557)  
 30 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 179) (SEQ ID NO:9558)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 180) (SEQ ID NO:9559)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 181) (SEQ ID NO:9560)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT GG-3' (FRAG 182) (SEQ ID NO:9561)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 183) (SEQ ID NO:9562)  
 35 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 184) (SEQ ID NO:9563)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 185) (SEQ ID NO:9564)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG C-3' (FRAG 186) (SEQ ID NO:9565)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CGG -3' (FRAG 187) (SEQ ID NO:9566)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG CG -3' (FRAG 188) (SEQ ID NO:9567)  
 40 5'-GGC CTG GAA AGC TGA GAT GGA GGG C -3' (FRAG 189) (SEQ ID NO:9568)  
 5'-GGC CTG GAA AGC TGA GAT GGA GGG -3' (FRAG 190) (SEQ ID NO:9569)  
 5'-GGC CTG GAA AGC TGA GAT GGA GG -3' (FRAG 191) (SEQ ID NO:9570)  
 5'-GGC CTG GAA AGC TGA GAT GGA G -3' (FRAG 192) (SEQ ID NO:9571)  
 5'-GGC CTG GAA AGC TGA GAT GGA -3' (FRAG 193) (SEQ ID NO:9572)  
 45 5'-GGC CTG GAA AGC TGA GAT GG -3' (FRAG 194) (SEQ ID NO:9573)  
 5'-GGC CTG GAA AGC TGA GAT G -3' (FRAG 195) (SEQ ID NO:9574)  
 5'-GGC CTG GAA AGC TGA GAT -3' (FRAG 196) (SEQ ID NO:9575)  
 5'-GGC CTG GAA AGC TGA GA-3' (FRAG 197) (SEQ ID NO:9576)  
 5'-GGC CTG GAA AGC TGA G-3' (FRAG 198) (SEQ ID NO:9577)  
 50 5'-GGC CTG GAA AGC TGA-3' (FRAG 199) (SEQ ID NO:9578)  
 5'-GGC CTG GAA AGC TG-3' (FRAG 200) (SEQ ID NO:9579)  
 5'-GGC CTG GAA AGC T-3' (FRAG 201) (SEQ ID NO:9580)  
 5'-GGC CTG GAA AGC-3' (FRAG 202) (SEQ ID NO:9581)  
 5'-GGC CTG GAA AG-3' (FRAG 203) (SEQ ID NO:9582)  
 55 5'-GGC CTG GAA A-3' (FRAG 204) (SEQ ID NO:9583)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 205) (SEQ ID NO:9584)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 206) (SEQ ID NO:9585)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 207) (SEQ ID NO:9586)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 208) (SEQ ID NO:9587)  
 60 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 209) (SEQ ID NO:9588)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 210) (SEQ ID NO:9589)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 211) (SEQ ID NO:9590)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 212) (SEQ ID NO:9591)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 213) (SEQ ID NO:9592)  
 65 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 214) (SEQ ID NO:9593)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 215) (SEQ ID NO:9594)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 216) (SEQ ID NO:9595)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 217) (SEQ ID NO:9596)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 218) (SEQ ID NO:9597)  
 70 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 219) (SEQ ID NO:9598)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 220) (SEQ ID NO:9599)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 221) (SEQ ID NO:9600)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 222) (SEQ ID NO:9601)  
 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 223) (SEQ ID NO:9602)  
 75 5'-GC CTG GAA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 224) (SEQ ID NO:9603)

- 5'- GC CTG GAA AGC TGA GAT GGA GGG CGG C-3' (FRAG 225) (SEQ ID NO:9604)  
5'- GC CTG GAA AGC TGA GAT GGA GGG CGG -3' (FRAG 226) (SEQ ID NO:9605)  
5'- GC CTG GAA AGC TGA GAT GGA GGG CG -3' (FRAG 227) (SEQ ID NO:9606)  
5'- GC CTG GAA AGC TGA GAT GGA GGG C -3' (FRAG 228) (SEQ ID NO:9607)  
5 5'- GC CTG GAA AGC TGA GAT GGA GGG -3' (FRAG 229) (SEQ ID NO:9608)  
5'- GC CTG GAA AGC TGA GAT GGA GG -3' (FRAG 230) (SEQ ID NO:9609)  
5'- GC CTG GAA AGC TGA GAT GGA G -3' (FRAG 231) (SEQ ID NO:9610)  
5'- GC CTG GAA AGC TGA GAT GGA -3' (FRAG 232) (SEQ ID NO:9611)  
5'- GC CTG GAA AGC TGA GAT GG -3' (FRAG 233) (SEQ ID NO:9612)  
10 5'- GC CTG GAA AGC TGA GAT G -3' (FRAG 234) (SEQ ID NO:9613)  
5'- GC CTG GAA AGC TGA GAT -3' (FRAG 235) (SEQ ID NO:9614)  
5'- GC CTG GAA AGC TGA GA-3' (FRAG 236) (SEQ ID NO:9615)  
5'- GC CTG GAA AGC TGA G-3' (FRAG 237) (SEQ ID NO:9616)  
5'- GC CTG GAA AGC TGA-3' (FRAG 238) (SEQ ID NO:9617)  
15 5'- GC CTG GAA AGC TG-3' (FRAG 239) (SEQ ID NO:9618)  
5'- GC CTG GAA AGC T-3' (FRAG 240) (SEQ ID NO:9619)  
5'- GC CTG GAA AGC-3' (FRAG 241) (SEQ ID NO:9620)  
5'- GC CTG GAA AG-3' (FRAG 242) (SEQ ID NO:9621)  
5'- C CTG GAA AGC TGA GAT GG A GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 243) (SEQ ID NO:9622)  
20 5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 244) (SEQ ID NO:9623)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 245) (SEQ ID NO:9624)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 246) (SEQ ID NO:9625)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 247) (SEQ ID NO:9626)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 248) (SEQ ID NO:9627)  
25 5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 249) (SEQ ID NO:9628)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 250) (SEQ ID NO:9629)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 251) (SEQ ID NO:9630)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 252) (SEQ ID NO:9631)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 253) (SEQ ID NO:9632)  
30 5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 254) (SEQ ID NO:9633)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 255) (SEQ ID NO:9634)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 256) (SEQ ID NO:9635)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 257) (SEQ ID NO:9636)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 258) (SEQ ID NO:9637)  
35 5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 259) (SEQ ID NO:9638)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 260) (SEQ ID NO:9639)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 261) (SEQ ID NO:9640)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 262) (SEQ ID NO:9641)  
5'- C CTG GAA AGC TGA GAT GGA GGG CGG C-3' (FRAG 263) (SEQ ID NO:9642)  
40 5'- C CTG GAA AGC TGA GAT GGA GGG CGG -3' (FRAG 264) (SEQ ID NO:9643)  
5'- C CTG GAA AGC TGA GAT GGA GGG CG -3' (FRAG 265) (SEQ ID NO:9644)  
5'- C CTG GAA AGC TGA GAT GGA GGG C -3' (FRAG 266) (SEQ ID NO:9645)  
5'- C CTG GAA AGC TGA GAT GGA GGG -3' (FRAG 267) (SEQ ID NO:9646)  
5'- C CTG GAA AGC TGA GAT GGA GG -3' (FRAG 268) (SEQ ID NO:9647)  
45 5'- C CTG GAA AGC TGA GAT GGA G -3' (FRAG 269) (SEQ ID NO:9648)  
5'- C CTG GAA AGC TGA GAT GGA -3' (FRAG 270) (SEQ ID NO:9649)  
5'- C CTG GAA AGC TGA GAT GG -3' (FRAG 271) (SEQ ID NO:9650)  
5'- C CTG GAA AGC TGA GAT G -3' (FRAG 272) (SEQ ID NO:9651)  
5'- C CTG GAA AGC TGA GAT -3' (FRAG 273) (SEQ ID NO:9652)  
50 5'- C CTG GAA AGC TGA GA-3' (FRAG 274) (SEQ ID NO:9653)  
5'- C CTG GAA AGC TGA G-3' (FRAG 275) (SEQ ID NO:9654)  
5'- C CTG GAA AGC TGA-3' (FRAG 276) (SEQ ID NO:9655)  
5'- C CTG GAA AGC TG-3' (FRAG 277) (SEQ ID NO:9656)  
5'- C CTG GAA AGC T-3' (FRAG 278) (SEQ ID NO:9657)  
55 5'- C CTG GAA AGC-3' (FRAG 279) (SEQ ID NO:9658)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 280) (SEQ ID NO:9659)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 281) (SEQ ID NO:9660)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 282) (SEQ ID NO:9661)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 283) (SEQ ID NO:9662)  
60 5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 284) (SEQ ID NO:9663)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 285) (SEQ ID NO:9664)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 286) (SEQ ID NO:9665)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 287) (SEQ ID NO:9666)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 288) (SEQ ID NO:9667)  
65 5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 289) (SEQ ID NO:9668)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 290) (SEQ ID NO:9669)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 291) (SEQ ID NO:9670)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 292) (SEQ ID NO:9671)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 293) (SEQ ID NO:9672)  
70 5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 294) (SEQ ID NO:9673)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 295) (SEQ ID NO:9674)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 296) (SEQ ID NO:9675)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 297) (SEQ ID NO:9676)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 298) (SEQ ID NO:9677)  
75 5'- CTG GAA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 299) (SEQ ID NO:9678)

- 5'- CTG GAA AGC TGA GAT GGA GGG CGG C-3' (FRAG 300) (SEQ ID NO:9679)  
5'- CTG GAA AGC TGA GAT GGA GGG CGG -3' (FRAG 301) (SEQ ID NO:9680)  
5'- CTG GAA AGC TGA GAT GGA GGG CG -3' (FRAG 302) (SEQ ID NO:9681)  
5'- CTG GAA AGC TGA GAT GGA GGG C -3' (FRAG 303) (SEQ ID NO:9682)  
5 5'- CTG GAA AGC TGA GAT GGA GGG -3' (FRAG 304) (SEQ ID NO:9683)  
5'- CTG GAA AGC TGA GAT GGA GG -3' (FRAG 305) (SEQ ID NO:9684)  
5'- CTG GAA AGC TGA GAT GGA G -3' (FRAG 306) (SEQ ID NO:9685)  
5'- CTG GAA AGC TGA GAT GGA -3' (FRAG 307) (SEQ ID NO:9686)  
5'- CTG GAA AGC TGA GAT GG -3' (FRAG 308) (SEQ ID NO:9687)  
10 5'- CTG GAA AGC TGA GAT G -3' (FRAG 309) (SEQ ID NO:9688)  
5'- CTG GAA AGC TGA GAT -3' (FRAG 310) (SEQ ID NO:9689)  
5'- CTG GAA AGC TGA GA-3' (FRAG 311) (SEQ ID NO:9690)  
5'- CTG GAA AGC TGA G-3' (FRAG 312) (SEQ ID NO:9691)  
5'- CTG GAA AGC TGA-3' (FRAG 313) (SEQ ID NO:9692)  
15 5'- CTG GAA AGC TG-3' (FRAG 314) (SEQ ID NO:9693)  
5'- CTG GAA AGC T-3' (FRAG 315) (SEQ ID NO:9694)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 316) (SEQ ID NO:9695)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 317) (SEQ ID NO:9696)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 318) (SEQ ID NO:9697)  
20 5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 319) (SEQ ID NO:9698)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 320) (SEQ ID NO:9699)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 321) (SEQ ID NO:9700)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 322) (SEQ ID NO:9701)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 323) (SEQ ID NO:9702)  
25 5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 324) (SEQ ID NO:9703)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 325) (SEQ ID NO:9704)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 326) (SEQ ID NO:9705)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 327) (SEQ ID NO:9706)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 328) (SEQ ID NO:9707)  
30 5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 329) (SEQ ID NO:9708)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 330) (SEQ ID NO:9709)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 331) (SEQ ID NO:9710)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 332) (SEQ ID NO:9711)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 333) (SEQ ID NO:9712)  
35 5'- TG GAA AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 334) (SEQ ID NO:9713)  
5'- TG GAA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 335) (SEQ ID NO:9714)  
5'- TG GAA AGC TGA GAT GGA GGG CGG C-3' (FRAG 336) (SEQ ID NO:9715)  
5'- TG GAA AGC TGA GAT GGA GGG CGG -3' (FRAG 337) (SEQ ID NO:9716)  
5'- TG GAA AGC TGA GAT GGA GGG CG -3' (FRAG 338) (SEQ ID NO:9717)  
40 5'- TG GAA AGC TGA GAT GGA GGG C -3' (FRAG 339) (SEQ ID NO:9718)  
5'- TG GAA AGC TGA GAT GGA GGG -3' (FRAG 340) (SEQ ID NO:9719)  
5'- TG GAA AGC TGA GAT GGA GG -3' (FRAG 341) (SEQ ID NO:9720)  
5'- TG GAA AGC TGA GAT GGA G -3' (FRAG 342) (SEQ ID NO:9721)  
5'- TG GAA AGC TGA GAT GGA -3' (FRAG 343) (SEQ ID NO:9722)  
45 5'- TG GAA AGC TGA GAT GG -3' (FRAG 344) (SEQ ID NO:9723)  
5'- TG GAA AGC TGA GAT G -3' (FRAG 345) (SEQ ID NO:9724)  
5'- TG GAA AGC TGA GAT -3' (FRAG 346) (SEQ ID NO:9725)  
5'- TG GAA AGC TGA GA-3' (FRAG 347) (SEQ ID NO:9726)  
5'- TG GAA AGC TGA G-3' (FRAG 348) (SEQ ID NO:9727)  
50 5'- TG GAA AGC TGA-3' (FRAG 349) (SEQ ID NO:9728)  
5'- TG GAA AGC TG-3' (FRAG 350) (SEQ ID NO:9729)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 351) (SEQ ID NO:9730)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 352) (SEQ ID NO:9731)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 353) (SEQ ID NO:9732)  
55 5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 354) (SEQ ID NO:9733)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 355) (SEQ ID NO:9734)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 356) (SEQ ID NO:9735)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 357) (SEQ ID NO:9736)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 358) (SEQ ID NO:9737)  
60 5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 359) (SEQ ID NO:9738)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 360) (SEQ ID NO:9739)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 361) (SEQ ID NO:9740)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 362) (SEQ ID NO:9741)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 363) (SEQ ID NO:9742)  
65 5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 364) (SEQ ID NO:9743)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 365) (SEQ ID NO:9744)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 366) (SEQ ID NO:9745)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 367) (SEQ ID NO:9746)  
5'- G GAA AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 368) (SEQ ID NO:9747)  
70 5'- G GAA AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 369) (SEQ ID NO:9748)  
5'- G GAA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 370) (SEQ ID NO:9749)  
5'- G GAA AGC TGA GAT GGA GGG CGG C-3' (FRAG 371) (SEQ ID NO:9750)  
5'- G GAA AGC TGA GAT GGA GGG CGG -3' (FRAG 372) (SEQ ID NO:9751)  
5'- G GAA AGC TGA GAT GGA GGG CG -3' (FRAG 373) (SEQ ID NO:9752)  
75 5'- G GAA AGC TGA GAT GGA GGG C -3' (FRAG 374) (SEQ ID NO:9753)

- 5'- G GAA AGC TGA GAT GGA GGG -3' (FRAG 375) (SEQ ID NO:9754)  
 5'- G GAA AGC TGA GAT GGA GG -3' (FRAG 376) (SEQ ID NO:9755)  
 5'- G GAA AGC TGA GAT GGA G -3' (FRAG 377) (SEQ ID NO:9756)  
 5'- G GAA AGC TGA GAT GGA -3' (FRAG 378) (SEQ ID NO:9757)  
 5 5'- G GAA AGC TGA GAT GG -3' (FRAG 379) (SEQ ID NO:9758)  
 5'- G GAA AGC TGA GAT G -3' (FRAG 380) (SEQ ID NO:9759)  
 5'- G GAA AGC TGA GAT -3' (FRAG 381) (SEQ ID NO:9760)  
 5'- G GAA AGC TGA GA-3' (FRAG 382) (SEQ ID NO:9761)  
 5'- G GAA AGC TGA G-3' (FRAG 383) (SEQ ID NO:9762)  
 10 5'- G GAA AGC TGA-3' (FRAG 384) (SEQ ID NO:9763)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 385) (SEQ ID NO:9764)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 386) (SEQ ID NO:9765)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 387) (SEQ ID NO:9766)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 388) (SEQ ID NO:9767)  
 15 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 389) (SEQ ID NO:9768)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 390) (SEQ ID NO:9769)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 391) (SEQ ID NO:9770)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 392) (SEQ ID NO:9771)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 393) (SEQ ID NO:9772)  
 20 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 394) (SEQ ID NO:9773)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 395) (SEQ ID NO:9774)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 396) (SEQ ID NO:9775)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 397) (SEQ ID NO:9776)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 398) (SEQ ID NO:9777)  
 25 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 399) (SEQ ID NO:9778)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 400) (SEQ ID NO:9779)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 401) (SEQ ID NO:9780)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 402) (SEQ ID NO:9781)  
 5'- GAA AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 403) (SEQ ID NO:9782)  
 30 5'- GAA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 404) (SEQ ID NO:9783)  
 5'- GAA AGC TGA GAT GGA GGG CGG C-3' (FRAG 405) (SEQ ID NO:9784)  
 5'- GAA AGC TGA GAT GGA GGG CGG -3' (FRAG 406) (SEQ ID NO:9785)  
 5'- GAA AGC TGA GAT GGA GGG CG -3' (FRAG 407) (SEQ ID NO:9786)  
 5'- GAA AGC TGA GAT GGA GGG C -3' (FRAG 408) (SEQ ID NO:9787)  
 35 5'- GAA AGC TGA GAT GGA GGG -3' (FRAG 409) (SEQ ID NO:9788)  
 5'- GAA AGC TGA GAT GGA GG -3' (FRAG 410) (SEQ ID NO:9789)  
 5'- GAA AGC TGA GAT GGA G -3' (FRAG 411) (SEQ ID NO:9790)  
 5'- GAA AGC TGA GAT GGA -3' (FRAG 412) (SEQ ID NO:9791)  
 5'- GAA AGC TGA GAT GG -3' (FRAG 413) (SEQ ID NO:9792)  
 40 5'- GAA AGC TGA GAT G -3' (FRAG 414) (SEQ ID NO:9793)  
 5'- GAA AGC TGA GAT -3' (FRAG 415) (SEQ ID NO:9794)  
 5'- GAA AGC TGA GA-3' (FRAG 416) (SEQ ID NO:9795)  
 5'- GAA AGC TGA G-3' (FRAG 417) (SEQ ID NO:9796)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 418) (SEQ ID NO:9797)  
 45 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 419) (SEQ ID NO:9798)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 420) (SEQ ID NO:9799)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 421) (SEQ ID NO:9800)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 422) (SEQ ID NO:9801)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 423) (SEQ ID NO:9802)  
 50 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 424) (SEQ ID NO:9803)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 425) (SEQ ID NO:9804)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 426) (SEQ ID NO:9805)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 427) (SEQ ID NO:9806)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 428) (SEQ ID NO:9807)  
 55 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 429) (SEQ ID NO:9808)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 430) (SEQ ID NO:9809)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 431) (SEQ ID NO:9810)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 432) (SEQ ID NO:9811)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 433) (SEQ ID NO:9812)  
 60 5'- AA AGC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 434) (SEQ ID NO:9813)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 435) (SEQ ID NO:9814)  
 5'- AA AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 436) (SEQ ID NO:9815)  
 5'- AA AGC TGA GAT GGA GGG CGG CA-3' (FRAG 437) (SEQ ID NO:9816)  
 5'- AA AGC TGA GAT GGA GGG CGG C-3' (FRAG 438) (SEQ ID NO:9817)  
 65 5'- AA AGC TGA GAT GGA GGG CGG -3' (FRAG 439) (SEQ ID NO:9818)  
 5'- AA AGC TGA GAT GGA GGG CG -3' (FRAG 440) (SEQ ID NO:9819)  
 5'- AA AGC TGA GAT GGA GGG C -3' (FRAG 441) (SEQ ID NO:9820)  
 5'- AA AGC TGA GAT GGA GGG -3' (FRAG 442) (SEQ ID NO:9821)  
 5'- AA AGC TGA GAT GGA GG -3' (FRAG 443) (SEQ ID NO:9822)  
 70 5'- AA AGC TGA GAT GGA G -3' (FRAG 444) (SEQ ID NO:9823)  
 5'- AA AGC TGA GAT GGA -3' (FRAG 445) (SEQ ID NO:9824)  
 5'- AA AGC TGA GAT GG -3' (FRAG 446) (SEQ ID NO:9825)  
 5'- AA AGC TGA GAT G -3' (FRAG 447) (SEQ ID NO:9826)  
 5'- AA AGC TGA GAT -3' (FRAG 448) (SEQ ID NO:9827)  
 75 5'- AA AGC TGA GA-3' (FRAG 449) (SEQ ID NO:9828)

- 5'- A AGC TGA GAT GGA GGG CG G CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 450) (SEQ ID NO:9829)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 451) (SEQ ID NO:9830)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 452) (SEQ ID NO:9831)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 453) (SEQ ID NO:9832)  
 5 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 454) (SEQ ID NO:9833)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 455) (SEQ ID NO:9834)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 456) (SEQ ID NO:9835)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 457) (SEQ ID NO:9836)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 458) (SEQ ID NO:9837)  
 10 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 459) (SEQ ID NO:9838)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 460) (SEQ ID NO:9839)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 461) (SEQ ID NO:9840)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 462) (SEQ ID NO:9841)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 463) (SEQ ID NO:9842)  
 15 5'- A AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 464) (SEQ ID NO:9843)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 465) (SEQ ID NO:9844)  
 5'- A AGC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 466) (SEQ ID NO:9845)  
 5'- A AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 467) (SEQ ID NO:9846)  
 5'- A AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 468) (SEQ ID NO:9847)  
 20 5'- A AGC TGA GAT GGA GGG CGG CA-3' (FRAG 469) (SEQ ID NO:9848)  
 5'- A AGC TGA GAT GGA GGG CGG C-3' (FRAG 470) (SEQ ID NO:9849)  
 5'- A AGC TGA GAT GGA GGG CGG -3' (FRAG 471) (SEQ ID NO:9850)  
 5'- A AGC TGA GAT GGA GGG CG -3' (FRAG 472) (SEQ ID NO:9851)  
 5'- A AGC TGA GAT GGA GGG C -3' (FRAG 473) (SEQ ID NO:9852)  
 25 5'- A AGC TGA GAT GGA GGG -3' (FRAG 474) (SEQ ID NO:9853)  
 5'- A AGC TGA GAT GGA GG -3' (FRAG 475) (SEQ ID NO:9854)  
 5'- A AGC TGA GAT GGA G -3' (FRAG 476) (SEQ ID NO:9855)  
 5'- A AGC TGA GAT GGA -3' (FRAG 477) (SEQ ID NO:9856)  
 5'- A AGC TGA GAT GG -3' (FRAG 478) (SEQ ID NO:9857)  
 30 5'- A AGC TGA GAT G -3' (FRAG 479) (SEQ ID NO:9858)  
 5'- A AGC TGA GAT -3' (FRAG 480) (SEQ ID NO:9859)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 481) (SEQ ID NO:9860)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 482) (SEQ ID NO:9861)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 483) (SEQ ID NO:9862)  
 35 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 484) (SEQ ID NO:9863)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 485) (SEQ ID NO:9864)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 486) (SEQ ID NO:9865)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 487) (SEQ ID NO:9866)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 488) (SEQ ID NO:9867)  
 40 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 489) (SEQ ID NO:9868)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 490) (SEQ ID NO:9869)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 491) (SEQ ID NO:9870)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 492) (SEQ ID NO:9871)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 493) (SEQ ID NO:9872)  
 45 5'- AGC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 494) (SEQ ID NO:9873)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 495) (SEQ ID NO:9874)  
 5'- AGC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 496) (SEQ ID NO:9875)  
 5'- AGC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 497) (SEQ ID NO:9876)  
 5'- AGC TGA GAT GGA GGG CGG CAT G -3' (FRAG 498) (SEQ ID NO:9877)  
 50 5'- AGC TGA GAT GGA GGG CGG CAT -3' (FRAG 499) (SEQ ID NO:9878)  
 5'- AGC TGA GAT GGA GGG CGG CA-3' (FRAG 500) (SEQ ID NO:9879)  
 5'- AGC TGA GAT GGA GGG CGG C-3' (FRAG 501) (SEQ ID NO:9880)  
 5'- AGC TGA GAT GGA GGG CGG -3' (FRAG 502) (SEQ ID NO:9881)  
 5'- AGC TGA GAT GGA GGG CG -3' (FRAG 503) (SEQ ID NO:9882)  
 55 5'- AGC TGA GAT GGA GGG C -3' (FRAG 504) (SEQ ID NO:9883)  
 5'- AGC TGA GAT GGA GGG -3' (FRAG 505) (SEQ ID NO:9884)  
 5'- AGC TGA GAT GGA GG -3' (FRAG 506) (SEQ ID NO:9885)  
 5'- AGC TGA GAT GGA G -3' (FRAG 507) (SEQ ID NO:9886)  
 5'- AGC TGA GAT GGA -3' (FRAG 508) (SEQ ID NO:9887)  
 60 5'- AGC TGA GAT GG -3' (FRAG 509) (SEQ ID NO:9888)  
 5'- AGC TGA GAT G -3' (FRAG 510) (SEQ ID NO:9889)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 511) (SEQ ID NO:9890)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 512) (SEQ ID NO:9891)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 513) (SEQ ID NO:9892)  
 65 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 514) (SEQ ID NO:9893)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 515) (SEQ ID NO:9894)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 516) (SEQ ID NO:9895)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 517) (SEQ ID NO:9896)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 518) (SEQ ID NO:9897)  
 70 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 519) (SEQ ID NO:9898)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 520) (SEQ ID NO:9899)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 521) (SEQ ID NO:9900)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 522) (SEQ ID NO:9901)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 523) (SEQ ID NO:9902)  
 75 5'- GC TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 524) (SEQ ID NO:9903)



- 5'- GC TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 525) (SEQ ID NO:9904)  
 5'- GC TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 526) (SEQ ID NO:9905)  
 5'- GC TGA GAT GGA GGG CGG CAT GG -3' (FRAG 527) (SEQ ID NO:9906)  
 5'- GC TGA GAT GGA GGG CGG CAT G -3' (FRAG 528) (SEQ ID NO:9907)  
 5'- GC TGA GAT GGA GGG CGG CAT -3' (FRAG 529) (SEQ ID NO:9908)  
 5'- GC TGA GAT GGA GGG CGG CA-3' (FRAG 530) (SEQ ID NO:9909)  
 5'- GC TGA GAT GGA GGG CGG C-3' (FRAG 531) (SEQ ID NO:9910)  
 5'- GC TGA GAT GGA GGG CGG -3' (FRAG 532) (SEQ ID NO:9911)  
 5'- GC TGA GAT GGA GGG CG -3' (FRAG 533) (SEQ ID NO:9912)  
 10 5'- GC TGA GAT GGA GGG C -3' (FRAG 534) (SEQ ID NO:9913)  
 5'- GC TGA GAT GGA GGG -3' (FRAG 535) (SEQ ID NO:9914)  
 5'- GC TGA GAT GGA GG -3' (FRAG 536) (SEQ ID NO:9915)  
 5'- GC TGA GAT GGA G -3' (FRAG 537) (SEQ ID NO:9916)  
 5'- GC TGA GAT GGA -3' (FRAG 538) (SEQ ID NO:9917)  
 15 5'- GC TGA GAT GG -3' (FRAG 539) (SEQ ID NO:9918)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 540) (SEQ ID NO:9919)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 541) (SEQ ID NO:9920)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 542) (SEQ ID NO:9921)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 543) (SEQ ID NO:9922)  
 20 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 544) (SEQ ID NO:9923)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 545) (SEQ ID NO:9924)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 546) (SEQ ID NO:9925)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 547) (SEQ ID NO:9926)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 548) (SEQ ID NO:9927)  
 25 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 549) (SEQ ID NO:9928)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 550) (SEQ ID NO:9929)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 551) (SEQ ID NO:9930)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 552) (SEQ ID NO:9931)  
 5'- C TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 553) (SEQ ID NO:9932)  
 30 5'- C TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 554) (SEQ ID NO:9933)  
 5'- C TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 555) (SEQ ID NO:9934)  
 5'- C TGA GAT GGA GGG CGG CAT GG -3' (FRAG 556) (SEQ ID NO:9935)  
 5'- C TGA GAT GGA GGG CGG CAT G -3' (FRAG 557) (SEQ ID NO:9936)  
 5'- C TGA GAT GGA GGG CGG CAT -3' (FRAG 558) (SEQ ID NO:9937)  
 35 5'- C TGA GAT GGA GGG CGG CA-3' (FRAG 559) (SEQ ID NO:9938)  
 5'- C TGA GAT GGA GGG CGG C-3' (FRAG 560) (SEQ ID NO:9939)  
 5'- C TGA GAT GGA GGG CGG -3' (FRAG 561) (SEQ ID NO:9940)  
 5'- C TGA GAT GGA GGG CG -3' (FRAG 562) (SEQ ID NO:9941)  
 5'- C TGA GAT GGA GGG C -3' (FRAG 563) (SEQ ID NO:9942)  
 40 5'- C TGA GAT GGA GGG -3' (FRAG 564) (SEQ ID NO:9943)  
 5'- C TGA GAT GGA GG -3' (FRAG 565) (SEQ ID NO:9944)  
 5'- C TGA GAT GGA G -3' (FRAG 566) (SEQ ID NO:9945)  
 5'- C TGA GAT GGA -3' (FRAG 567) (SEQ ID NO:9946)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 568) (SEQ ID NO:9947)  
 45 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 569) (SEQ ID NO:9948)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 570) (SEQ ID NO:9949)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 571) (SEQ ID NO:9950)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 572) (SEQ ID NO:9951)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 573) (SEQ ID NO:9952)  
 50 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 574) (SEQ ID NO:9953)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 575) (SEQ ID NO:9954)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 576) (SEQ ID NO:9955)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 577) (SEQ ID NO:9956)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 578) (SEQ ID NO:9957)  
 55 5'- TGA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 579) (SEQ ID NO:9958)  
 5'- TGA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 580) (SEQ ID NO:9959)  
 5'- TGA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 581) (SEQ ID NO:9960)  
 5'- TGA GAT GGA GGG CGG CAT GGC G-3' (FRAG 582) (SEQ ID NO:9961)  
 5'- TGA GAT GGA GGG CGG CAT GGC -3' (FRAG 583) (SEQ ID NO:9962)  
 60 5'- TGA GAT GGA GGG CGG CAT GG -3' (FRAG 584) (SEQ ID NO:9963)  
 5'- TGA GAT GGA GGG CGG CAT G -3' (FRAG 585) (SEQ ID NO:9964)  
 5'- TGA GAT GGA GGG CGG CAT -3' (FRAG 586) (SEQ ID NO:9965)  
 5'- TGA GAT GGA GGG CGG CA-3' (FRAG 587) (SEQ ID NO:9966)  
 5'- TGA GAT GGA GGG CGG C-3' (FRAG 588) (SEQ ID NO:9967)  
 65 5'- TGA GAT GGA GGG CGG -3' (FRAG 589) (SEQ ID NO:9968)  
 5'- TGA GAT GGA GGG CG -3' (FRAG 590) (SEQ ID NO:9969)  
 5'- TGA GAT GGA GGG C -3' (FRAG 591) (SEQ ID NO:9970)  
 5'- TGA GAT GGA GGG -3' (FRAG 592) (SEQ ID NO:9971)  
 5'- TGA GAT GGA GG -3' (FRAG 593) (SEQ ID NO:9972)  
 70 5'- TGA GAT GGA G -3' (FRAG 594) (SEQ ID NO:9973)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 595) (SEQ ID NO:9974)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 596) (SEQ ID NO:9975)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 597) (SEQ ID NO:9976)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 598) (SEQ ID NO:9977)  
 75 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 599) (SEQ ID NO:9978)

- 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 600) (SEQ ID NO:9979)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 601) (SEQ ID NO:9980)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 602) (SEQ ID NO:9981)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 603) (SEQ ID NO:9982)  
 5 5'- GA GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 604) (SEQ ID NO:9983)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 605) (SEQ ID NO:9984)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 606) (SEQ ID NO:9985)  
 5'- GA GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 607) (SEQ ID NO:9986)  
 5'- GA GAT GGA GGG CGG CAT GGC GG-3' (FRAG 608) (SEQ ID NO:9987)  
 10 5'- GA GAT GGA GGG CGG CAT GGC G-3' (FRAG 609) (SEQ ID NO:9988)  
 5'- GA GAT GGA GGG CGG CAT GGC -3' (FRAG 610) (SEQ ID NO:9989)  
 5'- GA GAT GGA GGG CGG CAT GG -3' (FRAG 611) (SEQ ID NO:9990)  
 5'- GA GAT GGA GGG CGG CAT G -3' (FRAG 612) (SEQ ID NO:9991)  
 5'- GA GAT GGA GGG CGG CAT -3' (FRAG 613) (SEQ ID NO:9992)  
 15 5'- GA GAT GGA GGG CGG CA-3' (FRAG 614) (SEQ ID NO:9993)  
 5'- GA GAT GGA GGG CGG C-3' (FRAG 615) (SEQ ID NO:9994)  
 5'- GA GAT GGA GGG CGG -3' (FRAG 616) (SEQ ID NO:9995)  
 5'- GA GAT GGA GGG CG -3' (FRAG 617) (SEQ ID NO:9996)  
 5'- GA GAT GGA GGG C -3' (FRAG 618) (SEQ ID NO:9997)  
 20 5'- GA GAT GGA GGG -3' (FRAG 619) (SEQ ID NO:9998)  
 5'- GA GAT GGA GG -3' (FRAG 620) (SEQ ID NO:9999)  
 5'- A GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 621) (SEQ ID NO:10000)  
 5'- A GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 622) (SEQ ID NO:10001)  
 5'- A GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 623) (SEQ ID NO:10002)  
 25 5'- A GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 624) (SEQ ID NO:10003)  
 5'- A GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 625) (SEQ ID NO:10004)  
 5'- A GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 626) (SEQ ID NO:10005)  
 5'- A GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 627) (SEQ ID NO:10006)  
 5'- A GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 628) (SEQ ID NO:10007)  
 30 5'- A GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 629) (SEQ ID NO:10008)  
 5'- A GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 630) (SEQ ID NO:10009)  
 5'- A GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 631) (SEQ ID NO:10010)  
 5'- A GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 632) (SEQ ID NO:10011)  
 5'- A GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 633) (SEQ ID NO:10012)  
 35 5'- A GAT GGA GGG CGG CAT GGC GG-3' (FRAG 634) (SEQ ID NO:10013)  
 5'- A GAT GGA GGG CGG CAT GGC G-3' (FRAG 635) (SEQ ID NO:10014)  
 5'- A GAT GGA GGG CGG CAT GGC -3' (FRAG 636) (SEQ ID NO:10015)  
 5'- A GAT GGA GGG CGG CAT GG -3' (FRAG 637) (SEQ ID NO:10016)  
 5'- A GAT GGA GGG CGG CAT G -3' (FRAG 638) (SEQ ID NO:10017)  
 40 5'- A GAT GGA GGG CGG CAT -3' (FRAG 639) (SEQ ID NO:10018)  
 5'- A GAT GGA GGG CGG CA-3' (FRAG 640) (SEQ ID NO:10019)  
 5'- A GAT GGA GGG CGG C-3' (FRAG 641) (SEQ ID NO:10020)  
 5'- A GAT GGA GGG CGG -3' (FRAG 642) (SEQ ID NO:10021)  
 5'- A GAT GGA GGG CG -3' (FRAG 643) (SEQ ID NO:10022)  
 45 5'- A GAT GGA GGG C -3' (FRAG 644) (SEQ ID NO:10023)  
 5'- A GAT GGA GGG -3' (FRAG 645) (SEQ ID NO:10024)  
 5'- GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 646) (SEQ ID NO:10025)  
 5'- GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 647) (SEQ ID NO:10026)  
 5'- GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 648) (SEQ ID NO:10027)  
 50 5'- GAT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 649) (SEQ ID NO:10028)  
 5'- GAT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 650) (SEQ ID NO:10029)  
 5'- GAT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 651) (SEQ ID NO:10030)  
 5'- GAT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 652) (SEQ ID NO:10031)  
 5'- GAT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 653) (SEQ ID NO:10032)  
 55 5'- GAT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 654) (SEQ ID NO:10033)  
 5'- GAT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 655) (SEQ ID NO:10034)  
 5'- GAT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 656) (SEQ ID NO:10035)  
 5'- GAT GGA GGG CGG CAT GGC GGG C-3' (FRAG 657) (SEQ ID NO:10036)  
 5'- GAT GGA GGG CGG CAT GGC GGG -3' (FRAG 658) (SEQ ID NO:10037)  
 60 5'- GAT GGA GGG CGG CAT GGC GG-3' (FRAG 659) (SEQ ID NO:10038)  
 5'- GAT GGA GGG CGG CAT GGC G-3' (FRAG 660) (SEQ ID NO:10039)  
 5'- GAT GGA GGG CGG CAT GGC -3' (FRAG 661) (SEQ ID NO:10040)  
 5'- GAT GGA GGG CGG CAT GG -3' (FRAG 662) (SEQ ID NO:10041)  
 5'- GAT GGA GGG CGG CAT G -3' (FRAG 663) (SEQ ID NO:10042)  
 65 5'- GAT GGA GGG CGG CAT -3' (FRAG 664) (SEQ ID NO:10043)  
 5'- GAT GGA GGG CGG CA-3' (FRAG 665) (SEQ ID NO:10044)  
 5'- GAT GGA GGG CGG C-3' (FRAG 666) (SEQ ID NO:10045)  
 5'- GAT GGA GGG CGG -3' (FRAG 667) (SEQ ID NO:10046)  
 5'- GAT GGA GGG CG -3' (FRAG 668) (SEQ ID NO:10047)  
 70 5'- GAT GGA GGG C -3' (FRAG 669) (SEQ ID NO:10048)  
 5'- AT GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 670) (SEQ ID NO:10049)  
 5'- AT GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 671) (SEQ ID NO:10050)  
 5'- AT GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 672) (SEQ ID NO:10051)  
 5'- AT GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 673) (SEQ ID NO:10052)  
 75 5'- AT GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 674) (SEQ ID NO:10053)

- 5'- AT GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 675) (SEQ ID NO:10054)  
5'- AT GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 676) (SEQ ID NO:10055)  
5'- AT GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 677) (SEQ ID NO:10056)  
5'- AT GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 678) (SEQ ID NO:10057)  
5 5'- AT GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 679) (SEQ ID NO:10058)  
5'- AT GGA GGG CGG CAT GGC GGG CA-3' (FRAG 680) (SEQ ID NO:10059)  
5'- AT GGA GGG CGG CAT GGC GGG C-3' (FRAG 681) (SEQ ID NO:10060)  
5'- AT GGA GGG CGG CAT GGC GGG -3' (FRAG 682) (SEQ ID NO:10061)  
5'- AT GGA GGG CGG CAT GGC GG-3' (FRAG 683) (SEQ ID NO:10062)  
10 5'- AT GGA GGG CGG CAT GGC G-3' (FRAG 684) (SEQ ID NO:10063)  
5'- AT GGA GGG CGG CAT GGC -3' (FRAG 685) (SEQ ID NO:10064)  
5'- AT GGA GGG CGG CAT GG -3' (FRAG 686) (SEQ ID NO:10065)  
5'- AT GGA GGG CGG CAT G -3' (FRAG 687) (SEQ ID NO:10066)  
5'- AT GGA GGG CGG CAT -3' (FRAG 688) (SEQ ID NO:10067)  
15 5'- AT GGA GGG CGG CA-3' (FRAG 689) (SEQ ID NO:10068)  
5'- AT GGA GGG CGG C-3' (FRAG 690) (SEQ ID NO:10069)  
5'- AT GGA GGG CGG -3' (FRAG 691) (SEQ ID NO:10070)  
5'- AT GGA GGG CG -3' (FRAG 692) (SEQ ID NO:10071)  
5'- T GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 693) (SEQ ID NO:10072)  
20 5'- T GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 694) (SEQ ID NO:10073)  
5'- T GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 695) (SEQ ID NO:10074)  
5'- T GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 696) (SEQ ID NO:10075)  
5'- T GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 697) (SEQ ID NO:10076)  
5'- T GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 698) (SEQ ID NO:10077)  
25 5'- T GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 699) (SEQ ID NO:10078)  
5'- T GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 700) (SEQ ID NO:10079)  
5'- T GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 701) (SEQ ID NO:10080)  
5'- T GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 702) (SEQ ID NO:10081)  
5'- T GGA GGG CGG CAT GGC GGG CA-3' (FRAG 703) (SEQ ID NO:10082)  
30 5'- T GGA GGG CGG CAT GGC GGG C-3' (FRAG 704) (SEQ ID NO:10083)  
5'- T GGA GGG CGG CAT GGC GGG -3' (FRAG 705) (SEQ ID NO:10084)  
5'- T GGA GGG CGG CAT GGC GG-3' (FRAG 706) (SEQ ID NO:10085)  
5'- T GGA GGG CGG CAT GGC G-3' (FRAG 707) (SEQ ID NO:10086)  
5'- T GGA GGG CGG CAT GGC -3' (FRAG 708) (SEQ ID NO:10087)  
35 5'- T GGA GGG CGG CAT GG -3' (FRAG 709) (SEQ ID NO:10088)  
5'- T GGA GGG CGG CAT G -3' (FRAG 710) (SEQ ID NO:10089)  
5'- T GGA GGG CGG CAT -3' (FRAG 711) (SEQ ID NO:10090)  
5'- T GGA GGG CGG CA-3' (FRAG 712) (SEQ ID NO:10091)  
5'- T GGA GGG CGG C-3' (FRAG 713) (SEQ ID NO:10092)  
40 5'- T GGA GGG CGG -3' (FRAG 714) (SEQ ID NO:10093)  
5'- GGA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 715) (SEQ ID NO:10094)  
5'- GGA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 716) (SEQ ID NO:10095)  
5'- GGA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 717) (SEQ ID NO:10096)  
5'- GGA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 718) (SEQ ID NO:10097)  
45 5'- GGA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 719) (SEQ ID NO:10098)  
5'- GGA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 720) (SEQ ID NO:10099)  
5'- GGA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 721) (SEQ ID NO:10100)  
5'- GGA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 722) (SEQ ID NO:10101)  
5'- GGA GGG CGG CAT GGC GGG CAC A-3' (FRAG 723) (SEQ ID NO:10102)  
50 5'- GGA GGG CGG CAT GGC GGG CAC-3' (FRAG 724) (SEQ ID NO:10103)  
5'- GGA GGG CGG CAT GGC GGG CA-3' (FRAG 725) (SEQ ID NO:10104)  
5'- GGA GGG CGG CAT GGC GGG C-3' (FRAG 726) (SEQ ID NO:10105)  
5'- GGA GGG CGG CAT GGC GGG -3' (FRAG 727) (SEQ ID NO:10106)  
5'- GGA GGG CGG CAT GGC GG-3' (FRAG 728) (SEQ ID NO:10107)  
55 5'- GGA GGG CGG CAT GGC G-3' (FRAG 729) (SEQ ID NO:10108)  
5'- GGA GGG CGG CAT GGC -3' (FRAG 730) (SEQ ID NO:10109)  
5'- GGA GGG CGG CAT GG -3' (FRAG 731) (SEQ ID NO:10110)  
5'- GGA GGG CGG CAT G -3' (FRAG 732) (SEQ ID NO:10111)  
5'- GGA GGG CGG CAT -3' (FRAG 733) (SEQ ID NO:10112)  
60 5'- GGA GGG CGG CA-3' (FRAG 734) (SEQ ID NO:10113)  
5'- GGA GGG CGG C-3' (FRAG 735) (SEQ ID NO:10114)  
5'- GA GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 736) (SEQ ID NO:10115)  
5'- GA GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 737) (SEQ ID NO:10116)  
5'- GA GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 738) (SEQ ID NO:10117)  
65 5'- GA GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 739) (SEQ ID NO:10118)  
5'- GA GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 740) (SEQ ID NO:10119)  
5'- GA GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 741) (SEQ ID NO:10120)  
5'- GA GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 742) (SEQ ID NO:10121)  
5'- GA GGG CGG CAT GGC GGG CAC AG-3' (FRAG 743) (SEQ ID NO:10122)  
70 5'- GA GGG CGG CAT GGC GGG CAC A-3' (FRAG 744) (SEQ ID NO:10123)  
5'- GA GGG CGG CAT GGC GGG CAC-3' (FRAG 745) (SEQ ID NO:10124)  
5'- GA GGG CGG CAT GGC GGG CA-3' (FRAG 746) (SEQ ID NO:10125)  
5'- GA GGG CGG CAT GGC GGG C-3' (FRAG 747) (SEQ ID NO:10126)  
5'- GA GGG CGG CAT GGC GGG -3' (FRAG 748) (SEQ ID NO:10127)  
75 5'- GA GGG CGG CAT GGC GG-3' (FRAG 749) (SEQ ID NO:10128)

5'-	GA GGG CGG CAT GGC G-3' (FRAG 750) (SEQ ID NO:10129)
5'-	GA GGG CGG CAT GGC -3' (FRAG 751) (SEQ ID NO:10130)
5'-	GA GGG CGG CAT GG -3' (FRAG 752) (SEQ ID NO:10131)
5'-	GA GGG CGG CAT G -3' (FRAG 753) (SEQ ID NO:10132)
5	5'- GA GGG CGG CAT -3' (FRAG 754) (SEQ ID NO:10133)
5'-	GA GGG CGG CA-3' (FRAG 755) (SEQ ID NO:10134)
5'-	A GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 756) (SEQ ID NO:10135)
5'-	A GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 757) (SEQ ID NO:10136)
5'-	A GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 758) (SEQ ID NO:10137)
10	5'- A GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 759) (SEQ ID NO:10138)
5'-	A GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 760) (SEQ ID NO:10139)
5'-	A GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 761) (SEQ ID NO:10140)
5'-	A GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 762) (SEQ ID NO:10141)
5'-	A GGG CGG CAT GGC GGG CAC AG-3' (FRAG 763) (SEQ ID NO:10142)
15	5'- A GGG CGG CAT GGC GGG CAC A-3' (FRAG 764) (SEQ ID NO:10143)
5'-	A GGG CGG CAT GGC GGG CAC-3' (FRAG 765) (SEQ ID NO:10144)
5'-	A GGG CGG CAT GGC GGG CA-3' (FRAG 766) (SEQ ID NO:10145)
5'-	A GGG CGG CAT GGC GGG C-3' (FRAG 767) (SEQ ID NO:10146)
5'-	A GGG CGG CAT GGC GGG -3' (FRAG 768) (SEQ ID NO:10147)
20	5'- A GGG CGG CAT GGC GG-3' (FRAG 769) (SEQ ID NO:10148)
5'-	A GGG CGG CAT GGC G-3' (FRAG 770) (SEQ ID NO:10149)
5'-	A GGG CGG CAT GGC -3' (FRAG 771) (SEQ ID NO:10150)
5'-	A GGG CGG CAT GG -3' (FRAG 772) (SEQ ID NO:10151)
5'-	A GGG CGG CAT G -3' (FRAG 773) (SEQ ID NO:10152)
25	5'- A GGG CGG CAT -3' (FRAG 774) (SEQ ID NO:10153)
5'-	GGG CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 775) (SEQ ID NO:10154)
5'-	GGG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 776) (SEQ ID NO:10155)
5'-	GGG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 777) (SEQ ID NO:10156)
5'-	GGG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 778) (SEQ ID NO:10157)
30	5'- GGG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 779) (SEQ ID NO:10158)
5'-	GGG CGG CAT GGC GGG CAC AGG C-3' (FRAG 780) (SEQ ID NO:10159)
5'-	GGG CGG CAT GGC GGG CAC AGG -3' (FRAG 781) (SEQ ID NO:10160)
5'-	GGG CGG CAT GGC GGG CAC AG-3' (FRAG 782) (SEQ ID NO:10161)
5'-	GGG CGG CAT GGC GGG CAC A-3' (FRAG 783) (SEQ ID NO:10162)
35	5'- GGG CGG CAT GGC GGG CAC-3' (FRAG 784) (SEQ ID NO:10163)
5'-	GGG CGG CAT GGC GGG CA-3' (FRAG 785) (SEQ ID NO:10164)
5'-	GGG CGG CAT GGC GGG C-3' (FRAG 786) (SEQ ID NO:10165)
5'-	GGG CGG CAT GGC GGG -3' (FRAG 787) (SEQ ID NO:10166)
5'-	GGG CGG CAT GGC GG-3' (FRAG 788) (SEQ ID NO:10167)
40	5'- GGG CGG CAT GGC G-3' (FRAG 789) (SEQ ID NO:10168)
5'-	GGG CGG CAT GGC -3' (FRAG 790) (SEQ ID NO:10169)
5'-	GGG CGG CAT GG -3' (FRAG 791) (SEQ ID NO:10170)
5'-	GGG CGG CAT G -3' (FRAG 792) (SEQ ID NO:10171)
5'-	GG CGG CAT GGC GGG CAC AG G CTG GGC-3' (FRAG 793) (SEQ ID NO:10172)
45	5'- GG CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 794) (SEQ ID NO:10173)
5'-	GG CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 795) (SEQ ID NO:10174)
5'-	GG CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 796) (SEQ ID NO:10175)
5'-	GG CGG CAT GGC GGG CAC AGG CT-3' (FRAG 797) (SEQ ID NO:10176)
5'-	GG CGG CAT GGC GGG CAC AGG C-3' (FRAG 798) (SEQ ID NO:10177)
50	5'- GG CGG CAT GGC GGG CAC AGG -3' (FRAG 799) (SEQ ID NO:10178)
5'-	GG CGG CAT GGC GGG CAC AG-3' (FRAG 800) (SEQ ID NO:10179)
5'-	GG CGG CAT GGC GGG CAC A-3' (FRAG 801) (SEQ ID NO:10180)
5'-	GG CGG CAT GGC GGG CAC-3' (FRAG 802) (SEQ ID NO:10181)
5'-	GG CGG CAT GGC GGG CA-3' (FRAG 803) (SEQ ID NO:10182)
55	5'- GG CGG CAT GGC GGG C-3' (FRAG 804) (SEQ ID NO:10183)
5'-	GG CGG CAT GGC GGG -3' (FRAG 805) (SEQ ID NO:10184)
5'-	GG CGG CAT GGC GG-3' (FRAG 806) (SEQ ID NO:10185)
5'-	GG CGG CAT GGC G-3' (FRAG 807) (SEQ ID NO:10186)
5'-	GG CGG CAT GGC -3' (FRAG 808) (SEQ ID NO:10187)
60	5'- GG CGG CAT GG -3' (FRAG 809) (SEQ ID NO:10188)
5'-	G CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 810) (SEQ ID NO:10189)
5'-	G CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 811) (SEQ ID NO:10190)
5'-	G CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 812) (SEQ ID NO:10191)
5'-	G CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 813) (SEQ ID NO:10192)
65	5'- G CGG CAT GGC GGG CAC AGG CT-3' (FRAG 814) (SEQ ID NO:10193)
5'-	G CGG CAT GGC GGG CAC AGG C-3' (FRAG 815) (SEQ ID NO:10194)
5'-	G CGG CAT GGC GGG CAC AGG -3' (FRAG 816) (SEQ ID NO:10195)
5'-	G CGG CAT GGC GGG CAC AG-3' (FRAG 817) (SEQ ID NO:10196)
5'-	G CGG CAT GGC GGG CAC A-3' (FRAG 818) (SEQ ID NO:10197)
70	5'- G CGG CAT GGC GGG CAC-3' (FRAG 819) (SEQ ID NO:10198)
5'-	G CGG CAT GGC GGG CA-3' (FRAG 820) (SEQ ID NO:10199)
5'-	G CGG CAT GGC GGG C-3' (FRAG 821) (SEQ ID NO:10200)
5'-	G CGG CAT GGC GGG -3' (FRAG 822) (SEQ ID NO:10201)
5'-	G CGG CAT GGC GG-3' (FRAG 823) (SEQ ID NO:10202)
75	5'- G CGG CAT GGC G-3' (FRAG 824) (SEQ ID NO:10203)

5'- G CGG CAT GGC -3' (FRAG 825) (SEQ ID NO:10204)  
 5'- CGG CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 826) (SEQ ID NO:10205)  
 5'- CGG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 827) (SEQ ID NO:10206)  
 5'- CGG CAT GGC GGG CAC AGG CTG G-3' (FRAG 828) (SEQ ID NO:10207)  
 5 5'- CGG CAT GGC GGG CAC AGG CTG -3' (FRAG 829) (SEQ ID NO:10208)  
 5'- CGG CAT GGC GGG CAC AGG CT-3' (FRAG 830) (SEQ ID NO:10209)  
 5'- CGG CAT GGC GGG CAC AGG C-3' (FRAG 831) (SEQ ID NO:10210)  
 5'- CGG CAT GGC GGG CAC AGG -3' (FRAG 832) (SEQ ID NO:10211)  
 5'- CGG CAT GGC GGG CAC AG-3' (FRAG 833) (SEQ ID NO:10212)  
 10 5'- CGG CAT GGC GGG CAC A-3' (FRAG 834) (SEQ ID NO:10213)  
 5'- CGG CAT GGC GGG CAC-3' (FRAG 835) (SEQ ID NO:10214)  
 5'- CGG CAT GGC GGG CA-3' (FRAG 836) (SEQ ID NO:10215)  
 5'- CGG CAT GGC GGG C-3' (FRAG 837) (SEQ ID NO:10216)  
 5'- CGG CAT GGC GGG -3' (FRAG 838) (SEQ ID NO:10217)  
 15 5'- CGG CAT GGC GG-3' (FRAG 839) (SEQ ID NO:10218)  
 5'- CGG CAT GGC G-3' (FRAG 840) (SEQ ID NO:10219)  
 5'- GG CAT GGC GGG CAC AGG C TG GGC-3' (FRAG 841) (SEQ ID NO:10220)  
 5'- GG CAT GGC GGG CAC AGG CTG GG-3' (FRAG 842) (SEQ ID NO:10221)  
 5'- GG CAT GGC GGG CAC AGG CTG G-3' (FRAG 843) (SEQ ID NO:10222)  
 20 5'- GG CAT GGC GGG CAC AGG CTG -3' (FRAG 844) (SEQ ID NO:10223)  
 5'- GG CAT GGC GGG CAC AGG CT-3' (FRAG 845) (SEQ ID NO:10224)  
 5'- GG CAT GGC GGG CAC AGG C-3' (FRAG 846) (SEQ ID NO:10225)  
 5'- GG CAT GGC GGG CAC AGG -3' (FRAG 847) (SEQ ID NO:10226)  
 5'- GG CAT GGC GGG CAC AG-3' (FRAG 848) (SEQ ID NO:10227)  
 25 5'- GG CAT GGC GGG CAC A-3' (FRAG 849) (SEQ ID NO:10228)  
 5'- GG CAT GGC GGG CAC-3' (FRAG 850) (SEQ ID NO:10229)  
 5'- GG CAT GGC GGG CA-3' (FRAG 851) (SEQ ID NO:10230)  
 5'- GG CAT GGC GGG C-3' (FRAG 852) (SEQ ID NO:10231)  
 5'- GG CAT GGC GGG -3' (FRAG 853) (SEQ ID NO:10232)  
 30 5'- GG CAT GGC GG-3' (FRAG 854) (SEQ ID NO:10233)  
 5'- G CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 855) (SEQ ID NO:10234)  
 5'- G CAT GGC GGG CAC AGG CTG GG-3' (FRAG 856) (SEQ ID NO:10235)  
 5'- G CAT GGC GGG CAC AGG CTG G-3' (FRAG 857) (SEQ ID NO:10236)  
 5'- G CAT GGC GGG CAC AGG CTG -3' (FRAG 858) (SEQ ID NO:10237)  
 35 5'- G CAT GGC GGG CAC AGG CT-3' (FRAG 859) (SEQ ID NO:10238)  
 5'- G CAT GGC GGG CAC AGG C-3' (FRAG 860) (SEQ ID NO:10239)  
 5'- G CAT GGC GGG CAC AGG -3' (FRAG 861) (SEQ ID NO:10240)  
 5'- G CAT GGC GGG CAC AG-3' (FRAG 862) (SEQ ID NO:10241)  
 5'- G CAT GGC GGG CAC A-3' (FRAG 863) (SEQ ID NO:10242)  
 40 5'- G CAT GGC GGG CAC-3' (FRAG 864) (SEQ ID NO:10243)  
 5'- G CAT GGC GGG CA-3' (FRAG 865) (SEQ ID NO:10244)  
 5'- G CAT GGC GGG C-3' (FRAG 866) (SEQ ID NO:10245)  
 5'- G CAT GGC GGG -3' (FRAG 867) (SEQ ID NO:10246)  
 5'- CAT GGC GGG CAC AGG CTG GGC-3' (FRAG 868) (SEQ ID NO:10247)  
 45 5'- CAT GGC GGG CAC AGG CTG GG-3' (FRAG 869) (SEQ ID NO:10248)  
 5'- CAT GGC GGG CAC AGG CTG G-3' (FRAG 870) (SEQ ID NO:10249)  
 5'- CAT GGC GGG CAC AGG CTG -3' (FRAG 871) (SEQ ID NO:10250)  
 5'- CAT GGC GGG CAC AGG CT-3' (FRAG 872) (SEQ ID NO:10251)  
 5'- CAT GGC GGG CAC AGG C-3' (FRAG 873) (SEQ ID NO:10252)  
 50 5'- CAT GGC GGG CAC AGG -3' (FRAG 874) (SEQ ID NO:10253)  
 5'- CAT GGC GGG CAC AG-3' (FRAG 875) (SEQ ID NO:10254)  
 5'- CAT GGC GGG CAC A-3' (FRAG 876) (SEQ ID NO:10255)  
 5'- CAT GGC GGG CAC-3' (FRAG 877) (SEQ ID NO:10256)  
 5'- CAT GGC GGG CA-3' (FRAG 878) (SEQ ID NO:10257)  
 55 5'- CAT GGC GGG C-3' (FRAG 879) (SEQ ID NO:10258)  
 5'- AT GGC GGG CAC AGG CTG GGC-3' (FRAG 880) (SEQ ID NO:10259)  
 5'- AT GGC GGG CAC AGG CTG GG-3' (FRAG 881) (SEQ ID NO:10260)  
 5'- AT GGC GGG CAC AGG CTG G-3' (FRAG 882) (SEQ ID NO:10261)  
 5'- AT GGC GGG CAC AGG CTG -3' (FRAG 883) (SEQ ID NO:10262)  
 60 5'- AT GGC GGG CAC AGG CT-3' (FRAG 884) (SEQ ID NO:10263)  
 5'- AT GGC GGG CAC AGG C-3' (FRAG 885) (SEQ ID NO:10264)  
 5'- AT GGC GGG CAC AGG -3' (FRAG 886) (SEQ ID NO:10265)  
 5'- AT GGC GGG CAC AG-3' (FRAG 887) (SEQ ID NO:10266)  
 5'- AT GGC GGG CAC A-3' (FRAG 888) (SEQ ID NO:10267)  
 65 5'- AT GGC GGG CAC-3' (FRAG 889) (SEQ ID NO:10268)  
 5'- AT GGC GGG CA-3' (FRAG 890) (SEQ ID NO:10269)  
 5'- T GGC GGG CAC AGG CTG GGC-3' (FRAG 891) (SEQ ID NO:10270)  
 5'- T GGC GGG CAC AGG CTG GG-3' (FRAG 892) (SEQ ID NO:10271)  
 5'- T GGC GGG CAC AGG CTG G-3' (FRAG 893) (SEQ ID NO:10272)  
 70 5'- T GGC GGG CAC AGG CTG -3' (FRAG 894) (SEQ ID NO:10273)  
 5'- T GGC GGG CAC AGG CT-3' (FRAG 895) (SEQ ID NO:10274)  
 5'- T GGC GGG CAC AGG C-3' (FRAG 896) (SEQ ID NO:10275)  
 5'- T GGC GGG CAC AGG -3' (FRAG 897) (SEQ ID NO:10276)  
 5'- T GGC GGG CAC AG-3' (FRAG 898) (SEQ ID NO:10277)  
 75 5'- T GGC GGG CAC A-3' (FRAG 899) (SEQ ID NO:10278)

- 5'- T GGC GGG CAC -3' (FRAG 900) (SEQ ID NO:10279)  
 5'- GGC GGG CAC AGG CTG GGC -3' (FRAG 901) (SEQ ID NO:10280)  
 5'- GGC GGG CAC AGG CTG GG -3' (FRAG 902) (SEQ ID NO:10281)  
 5'- GGC GGG CAC AGG CTG G -3' (FRAG 903) (SEQ ID NO:10282)  
 5 5'- GGC GGG CAC AGG CTG -3' (FRAG 904) (SEQ ID NO:10283)  
 5'- GGC GGG CAC AGG CT -3' (FRAG 905) (SEQ ID NO:10284)  
 5'- GGC GGG CAC AGG C -3' (FRAG 906) (SEQ ID NO:10285)  
 5'- GGC GGG CAC AGG -3' (FRAG 907) (SEQ ID NO:10286)  
 5'- GGC GGG CAC AG -3' (FRAG 908) (SEQ ID NO:10287)  
 10 5'- GGC GGG CAC A -3' (FRAG 909) (SEQ ID NO:10288)  
 5'- GC GGG CAC AGG CTG GGC -3' (FRAG 910) (SEQ ID NO:10289)  
 5'- GC GGG CAC AGG CTG GG -3' (FRAG 911) (SEQ ID NO:10290)  
 5'- GC GGG CAC AGG CTG G -3' (FRAG 912) (SEQ ID NO:10291)  
 5'- GC GGG CAC AGG CTG -3' (FRAG 913) (SEQ ID NO:10292)  
 15 5'- GC GGG CAC AGG CT -3' (FRAG 914) (SEQ ID NO:10293)  
 5'- GC GGG CAC AGG C -3' (FRAG 915) (SEQ ID NO:10294)  
 5'- GC GGG CAC AGG -3' (FRAG 916) (SEQ ID NO:10295)  
 5'- GC GGG CAC AG -3' (FRAG 917) (SEQ ID NO:10296)  
 5'- C GGG CAC AGG CTG GGC -3' (FRAG 918) (SEQ ID NO:10297)  
 20 5'- GGG CAC AGG CTG GG -3' (FRAG 919) (SEQ ID NO:10298)  
 5'- C GGG CAC AGG CTG G -3' (FRAG 920) (SEQ ID NO:10299)  
 5'- C GGG CAC AGG CTG -3' (FRAG 921) (SEQ ID NO:10300)  
 5'- C GGG CAC AGG CT -3' (FRAG 922) (SEQ ID NO:10301)  
 5'- C GGG CAC AGG C -3' (FRAG 923) (SEQ ID NO:10302)  
 25 5'- C GGG CAC AGG -3' (FRAG 924) (SEQ ID NO:10303)  
 5'- GGG CAC AGG CTG GGC -3' (FRAG 925) (SEQ ID NO:10304)  
 5'- GGG CAC AGG CTG GG -3' (FRAG 926) (SEQ ID NO:10305)  
 5'- GGG CAC AGG CTG G -3' (FRAG 927) (SEQ ID NO:10306)  
 5'- GGG CAC AGG CTG -3' (FRAG 928) (SEQ ID NO:10307)  
 30 5'- GGG CAC AGG CT -3' (FRAG 929) (SEQ ID NO:10308)  
 5'- GGG CAC AGG C -3' (FRAG 930) (SEQ ID NO:10309)  
 5'- GG CAC AGG CTG GGC -3' (FRAG 931) (SEQ ID NO:10310)  
 5'- GG CAC AGG CTG GG -3' (FRAG 932) (SEQ ID NO:10311)  
 5'- GG CAC AGG CTG G -3' (FRAG 933) (SEQ ID NO:10312)  
 35 5'- GG CAC AGG CTG -3' (FRAG 934) (SEQ ID NO:10313)  
 5'- GG CAC AGG CT -3' (FRAG 935) (SEQ ID NO:10314)  
 5'- G CAC AGG CTG GGC -3' (FRAG 936) (SEQ ID NO:10315)  
 5'- G CAC AGG CTG GG -3' (FRAG 937) (SEQ ID NO:10316)  
 5'- G CAC AGG CTG G -3' (FRAG 938) (SEQ ID NO:10317)  
 40 5'- G CAC AGG CTG -3' (FRAG 939) (SEQ ID NO:10318)  
 5'- CAC AGG CTG GGC -3' (FRAG 940) (SEQ ID NO:10319)  
 5'- CAC AGG CTG GG -3' (FRAG 941) (SEQ ID NO:10320)  
 5'- CAC AGG CTG G -3' (FRAG 942) (SEQ ID NO:10321)  
 5'- AC AGG CTG GGC -3' (FRAG 943) (SEQ ID NO:10322)  
 45 5'- AC AGG CTG GG -3' (FRAG 944) (SEQ ID NO:10323)  
 5'- C AGG CTG GGC -3' (FRAG 945) (SEQ ID NO:10324)  
 5'- TTT TCC TTC CTT TGT CTC TCT TC (FRAG 946) (SEQ ID NO:10325)  
 5'- GCT CCC GGC TGC CTG (FRAG 947) (SEQ ID NO:10326)  
 5'- CTC GGC CGT GCG GCT CTG TCG CTC CCG GT (FRAG 948) (SEQ ID NO:10327)  
 50 5'- CCG CCG CCC TCC GGG GGG TC (FRAG 949) (SEQ ID NO:10328)  
 5'- TGC TGC CGT TGG CTG CCC (FRAG 950) (SEQ ID NO:10329)  
 5'- CTT CTG CGG GTC GCC GG (FRAG 951) (SEQ ID NO:10330)  
 5'- TGC TGG GCT TGT GGC (FRAG 952) (SEQ ID NO:10331)  
 5'- GGC CTC TCT TCT GGG (FRAG 953) (SEQ ID NO:10332)  
 55 5'- CCT GGT CCC TCC GT (FRAG 954) (SEQ ID NO:10333)  
 5'- GGT GGC TCC TCT GC (FRAG 955) (SEQ ID NO:10334)  
 5'- GCT TGG TCC TGG GGC TGC (FRAG 956) (SEQ ID NO:10335)  
 5'- TGC TCT CCT CTC CTT (FRAG 957) (SEQ ID NO:10336)

#### **Human Adenosine A2a Receptor Nucleic Acid and Antisense Oligonucleotide Fragments**

- 60 5'- TGC TTT TCT TTT CTG GGC CTC TGT GGT CTG TTT TTT TCT G GCC CTG CTG GGG CGC TCT CC GCC GCC CGC CTG GCT  
 CCC GGB GCC CBT GBT GGG CBT GCC GTG GTT CTT GCC CTC CTT TGG CTG CCG TGC CCG CTC CCC GGC CTC CTG GCG GGT  
 GGC CGT TG GGC CCG TGT TCC CCT GGG -GCC TGG GGC TCC CTT CTC TC GCC CTT CTT GCT GGG CCT C TGC TGC TGC TGG  
 TGC TGT GGC CCC C GTA CAC CGA GGA GCC CAT GAT GGG CAT GCC ACA GAC GAC AGG C GTB CBC CGB GGB GCC CBT  
 GBT GGG CBT GCC BCB GBC GBC BGG C -3' (FRAG. NO. 1665) (SEQ ID NO:11049)  
 65 5'- CTG GGC CTC -3' (FRAG 1666) (SEQ ID NO:11050)  
 5'- TGC TTT TCT TTT CTG GGC CTC -3' (FRAG 958) (SEQ ID NO:10337)  
 5'- TGT GGT CTG TTT TTT TCT G -3' (FRAG 959) (SEQ ID NO:10338)  
 5'- GCC CTG CTG GGG CGC TCT CC -3' (FRAG 960) (SEQ ID NO:10339)  
 5'- GCC GCC CGC CTG GCT CCC -3' (FRAG 961) (SEQ ID NO:10340)  
 70 5'- GGB GCC CBT GBT GGG CBT GCC -3' (FRAG 962) (SEQ ID NO:10341)  
 5'- GTG GTT CTT GCC CTC CTT TGG CTG -3' (FRAG 963) (SEQ ID NO:10342)  
 5'- CCG TGC CCG CTC CCC GGC -3' (FRAG 964) (SEQ ID NO:10343)  
 5'- CTC CTG GCG GGT GGC CGT TG -3' (FRAG 965) (SEQ ID NO:10344)  
 5'- GGC CCG TGT TCC CCT GGG -3' (FRAG 966) (SEQ ID NO:10345)  
 75 5'- GCC TGG GGC TCC CTT CTC TC -3' (FRAG 967) (SEQ ID NO:10346)



5'-GCC CTT CTT GCT GGG CCT C-3' (FRAG 968) (SEQ ID NO:10347)

5'-TGC TGC TGC TGG TGC TGT GGC CCC C-3' (FRAG 969) (SEQ ID NO:10348)

5'-GTACACCGAGGAGCCCATGATGGGCATGCCACAGACGACAGGC-3' (FRAG 970) (SEQ ID NO:10349)

5'-GTBCBCCBGBGCCCCBTGTTGGGCBTGCBCBGBCBGCGC-3' (FRAG 971) (SEQ ID NO:10350)

**5 Human Adenosine A2b Receptor Nucleic Acid & Antisense Oligonucleotide Fragments**

5'-GGC GCC GTG CCG CGT CTT GGT GGC GGC GG GTT CGC GCC CGC GCG GGG CCC CTC CGG TCC GTT CGC GCC CGC GCG  
 GGG CCC CTC CGG TCC CGG GTC GGG GCC CCC CGC GGC C GCC TCG GGG CTG GGG CGC TGG TGG CCG GG CCG CGC CTC  
 CGC CTG CCG CTT CTG GCT GGG CCC CGG GCG CCC CCT CCC CTC TTG CTC GGG TCC CCG TG ACA GCG CGT CCT GTG TCT  
 CCA GCA GCA TGG CCG GGC CAG CTG GGC CCC BCB GCG CGT CCT GTG TCT CCB GCB GCB TGG CCG GGC CBG CTG GGC  
 10 CCC CCCAGCCCCG AGGCTCAGAA GCGGCAGGCG GAGGCGCGGT CCGGGCGCTA TGGCCATGCC CGCGGGTCT  
 CACGCGGGTG CCCTCGCCC GGCGCGCCTT CGGTAGGGGG CGCCCGGGGC CCAGCTGGCC CGGCCATGCT CTGGAGACA  
 CAGGACGCGC TGTACGTGGC GCTGGAGCTG GTCATCGCCG CGCTTTCGGT GCGGGGCAAC GTGCTGTGT GCGCCGCGGT  
 GGGCAGCGGC AACACTCTGC AGACGCCAC CAACTACTTC CTGGTGTCCT TGGCTGCGGC CGACGTGGCC GTGGGGTCT  
 TCGCCATCCA CTTTGCCATC ACCATCAGCC TGGGCTCTG CACTGACTTC TACGGCTGCC TCTTCTCGC GTGCTGTGT  
 15 CTGGTGCTCA CGCAGAGCTC CATCTTCAGC CTCTGCGCG TGGCAGTCGA CAGATACCTG GCCATCTGTG TCCCGCTCAG  
 GTATAAAAGT TTGTACACGG GGACCCGAGC AAGAGGGGTC ATTGCTGTCC TCTGGGTCTT TGCCTTTGGC ATCGGATTGA  
 CTCCATTCCT GGGGTGGAAC AGTAAAGACA GTGCCACCA CACTGCACA GAACCTGGG ATGGAACCA GAATGAAAGC  
 TGCTGCCTG TGAAGTGCT CTTTGAAGA GTGGTCCCA TGAGTACAT GGTATATTT GATATATTT GGTGTGTCT  
 GCCCCACTG CTTATAATGC TGGTGATCTA CATTAGATC TTCTGTGGT CCTGCAGGCA GCTTCAGCGC ACTGAGCTGA  
 20 TGGACCACTC GAGGACCACC CTCACGCGGG AGATCCATGC AGCCAAAGTCA CTGGCCATGA TTGTGGGAT TTTTGCCTG  
 TGCTGGTTC CTGTGCATGC TGTTAACTGT GTCACCTTT TCCAGCCAGC TCAGGGTAAA AATAAGCCCA AGTGGGCAAT  
 GAATATGGCC ATTCTTCTGT CACATGCCAA TTCACTGTGC ATATCCATTG TCTATGCTTA CCGGAACCGA GACTTCCGCT  
 ACACTTTTCA CAAAATTATC TCCAGGTATC TTCTCTGCCA AGCAGATGTC AAGAGTGGGA ATGTCAGGC TGGGGTACAG  
 CCTGCTCTCG GTGTGGGCTT ATGATCTAGG CTCTCGCCTC TTCCAGGAGA AGATACAAAT CCACAAGAAA CAAAGAGGAC  
 25 ACGGCTGGTT TTCATTGTGA AAGATAGCTA CACCTGCACA GGAAATGGAC TGCCTCTCTT GAGCACTTC CTGGAGCTAC  
 CACGTATCTA GCTAATATGT ATGTGTCAGT AGTAGCACA AGGATTGACA AATATATTTA TGATCTATTC AGTGTCTTTT  
 ACTGTGTGGA TTATGCCAAC AGCTTGAATG GATTCTAACA GACTCTTTTG TTTTAAAAAG TCTGCCTTGT TTATGGTGGA  
 AAATACTGA AACTATTITA CTGTGAAACA GTGTGAACCA TTATAATGCA AATACTTTT AACTTAGAG CAATGGAATA  
 AAAAAAGTG ACTGTACTAA AAATGTATAC TTGTGTCCAG GAAAGTGACC TCAAAAAATTA AAAGTATAAT TATTCGGCCG  
 30 GGCATGGTGG CTCACACCTG TAATCCAGC ACTTTGGGAG GCCAAGGCAG GCGGATCAGC AGGTACAGGAG TTCAAAACCA  
 GCGTGTCAA TATAGT GGCCAATTG TTAGTTATCC GCGGCCACA AGACGCGGCA CGGCGCCTGG ACCGGAGGGG  
 CCGCGCGCG GCGCAACTT TGGGCTCGGG CGAGTGGGTG GTGCTCCGCC CAGCCCGAGA CCGCGGGGCG CGCGGGCCAA  
 TGGGTGCCGC CTCTGGCCG CGGGGGGCGC CGACCCGTGG GTCCCGGCA CCAGCGCCCC AGCCCGAGG CTCAGAAGCG  
 GCAAGCGGAG GCGCGTCCG GCGGCTATGG CCATGCCCCG CGGGTCTCAC GCGGTGCCC CTCGCCCGC GCGCCTTCGG  
 35 TAGGGGGCGC CCGGGGCCCC GCTGGCCCCG CCATGCTGCT GGAGACACAG GACGCGCTGT ACGTGGCGT GAGTGTGCT  
 ATCGCCGCGG TTTCGGTGGC GGGCAACGTC CTGGTGTGCG CGCGGTGGG CACGCGGAAC ACTCTGCAGA CGCCCACTA  
 CTACTTCTG GTGTCCCTGG CTGCGGCCG CGTGCCGTG GGGCTCTCG CCATCCCTT TGCCATCACC ATCAGCCTGG  
 GCTTCTGCAC TGACTTCTAC GGCTGCTCT CTCTGCTGT CTCTGCTGT GTGCTACGC AGAGCTCCAT CTTCAGCCTT  
 CTGGCCGTGG CAGTCAGAC ATACCTGGCC ATCTGTGTC GTGCTGTC TAAAGTTTG GTACCGGGA CCCGAGGAGA  
 40 AGGGGTCTT CTGTCTCTT GGTCTCTG CTTTGGCATC GGATTGACTC CATTCTGGG GTGGAACAGT AAAGACAGTG  
 CCACCAACAA CTGCACAGAA CCCTGGGATG GAACACAGAA TGAAAGCTGC TGCCTTGTGA AGTGTCTCT TGAGAAATGT  
 TGCCCATGAG GCTACATGCT ATATTTCAAT TTCTTTGGT GTGTTCTGCC CCCACTGCTT ATAATGCTG TGATCTACAT  
 TAAGATCTT CTGGTGGCTT GCAGGCAGCT TCAGCGCACT GAGCTGATGG ACCACTCGAG GACCACCTC CAGCGGGAGA  
 45 TCCATGCAGC CAAGTCACTG GCCATGATTG TGGGGATTTT TGCCCTGTG TGGTTACCTG TGATGCTGT TAACTGTGTC  
 ACTCTTTTCC AGCCAGCTCA GGTAAAAAT AAGCCCAAGT GGGCAATGAA TATGGCCATT CTCTGTGAC ATGCCAATTC  
 AGTTGTCAAT CCCATTGCT ATGCTTACC GAACCGAGC TTCGCTACA CTTTTCACAA AATTATCTC AGGTATCTTC  
 TGTGCCAAG AGATGTCAAG AGTGGAATG GTCAGGCTGG GTCACAGCCT GCTCTCGGTG TGGGCTATG ATCTAGGCTC  
 TCGCCTCTC CAGGAGAAGA TACAAATCCA CAAGAAACAA AGAGGACACG GCTGGTTTTC ATTGTAAAG ATAGCTACAC  
 CTCACAAGGA AATGGACTGC CTCTCTGAG CACTTCCCTG GAGCTACCAC GTATCTAGCT AATATGTATG TGTAGTAGT  
 50 AGGCTCCAAG GATTGACAAA TATATTATG ATCTATTAC CTGCTTTTAC TGTGTGGATT ATGCCAACAG CTGAAATGGA  
 TTCTAACAGA CTCTTTTGT TTAAAAAGTC TGCTTGTIT ATGGTGGAAA ATTACTGAAA CTATTTTACT GTGAAACAGT  
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 35 5'-GCT GGG CCC CGG-3' (FRAG. NO: 1672) (SEQ ID NO:11056)  
 5'-CGG GTC GGG GCC CCC C-3' (FRAG. NO: 1673) (SEQ ID NO:11057)  
 5'-CGC GCC CGC G-3' (FRAG. NO: 1674) (SEQ ID NO:11058)  
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 40 5'-GTT CGC GCC CGC GCG GGG CCC CTC CGG TCC-3' (FRAG 974) (SEQ ID NO:10353)  
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 45 5'-CCC CTC TTG CTC GGG TCC CCG TG-3' (FRAG 979) (SEQ ID NO:10358)  
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 5'-BCBGGCGCTCTGTGTCTCCBGCBCBTGGCCGGCCBGCTGGGCCCC-3' (FRAG 981) (SEQ ID NO:10360)  
**Human Adenosine A3 Receptor Nucleic Acid and Antisense Oligonucleotide Fragments**  
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GGGAAGACCT CTGGCGAGAG CTAGGCCAC TGGCCCTACA CAGGGATCTT GCTGGCTCAC CTGTCCCTGT OGAGGTTCCT  
45 CTGGGAAGGC AAGATGCCCA ACAACAGCAC TGCTCTGTCA TTGGCCAATG TTACCTACAT CACCATGGAA ATTTTCATTG  
GACTCTGCGC CATAGTGGG AACGTGCTGG TCATCTGCTT GGTCAAGCTG AACCCAGCC TGCAGACCA CACCTTCTAT  
TTCAATGTCT CTCTAGCCCT GGCTGACATT GCTGTGGGG TGCTGGTCAT GCCTTTGGCC ATTGTGTGCA GCCTGGGCAT  
CACAATCCAC TTCTACAGCT GCCTTTTAT GACTTGCCTA CTGCTTATCT TTACCCACGC CTCCATCATG TCCTTGCTGG  
CCATCGCTGT GGACGATAC TTGCGGGTCA AGCTTACCGT CAGATACAAG AGGGTCACCA CTCACAGAAG AATATGGCTG  
GCCCTGGGCT TTGCTGGCT GGTGTCTTC CTGCTGGGAT TGACCCCAT GTTTGGCTGG AACATGAACT TGACCTCAGA  
50 GTACCAAGAG AATGTACCT TCCCTTTCATG CCAATTTGTT TCCGTCTAGA GGATGGACTA CATGGTATAC TTCAGCTTCC  
TCACCTGGAT TTTCATCCCC CTGGTTGTCA TGTGCGCAT CTATCTTGAC ATCTTTTACA TCATTGCGAA CAAACTCAGT  
CTGAACCTTAT CTAACCTCAA AGAGACAGGT GCATTTTATG GACGGGAGT CAAGACGGCT AAGTCTTGT TTCTGGTTCT  
TTTCTTGTT GCTCTGTCAT GGCTGCCCTT ATCTCTCAT AACTGATCA TCTACTTTAA TGTGAGGTA CCACAGGCTG  
TGCTGTACAT GGGCATCTG CTGTCCCATG CCAACTCCAT GATGAACCT ATCGTCTATG CCTATAAAAT AAAGAAGTTC  
55 AAGGAAACCT ACCTTTTAT CCTCAAAGCC TGTGTGGTCT GCCATCCCTC TGATTCTTG GACACAAGCA TTGAGAAGAA  
TTCTGAGTAG TTATCCATCA GAGATGACTT TGCTCATG ACCTTCAGAT TCCCCATCAA CAAACACTTG AGGGCTGTA  
TGCCGTAGGCC AAGGATTTT TACATCCTTG ATTACTTCCA CTGAGGTGGG AGCATCTCCA GTGCTCCCCA ATTATATCTC  
CCCCACTCCA CTACTCTCTT CCTCCACTTC ATTTTCTCTT TGCTCTTCT CTCTAATCA GTGTTTGGG GGCCTGACTT  
GGGGACAACG TATTATTGAT ATTATTGTCT GTTTTCTTC TTCCCAATAG AAGAATAAGT CATGGAGCCT GAAGGGTGCC  
60 TAGTTGACTT ACTGACAAA GGCTCTAGTT GGGCTGAACA TGTGTGTGGT GGTGACTCAT TTCCATGCCA TTGTGGAATT  
GAGCAGAGAA CTGCTCTCG GAGGATGCCT AGGAGATGTT GGGAAACAGAA GAAATAAACT GAGTTTAAGG GGGACTTAAA  
CTGCTGAATT C -3' (FRAG. NO.:) (SEQ ID NO:11796)  
5'-TTCCAG ATGGGCAGAG GTGGCTGGG TGGTGACCCT AAGTGTGTCT CCTGCCTTTA TTCTCTCTAG TGGGTTATTC  
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65 GACTGATTCC AAAAGAACTC ACCTATGTAC TGGGGTAGGG GAGGGAGGGT TTTTGCAGT ATTTAACTAA GGTTCAAAAGA  
GTGCTATATA GTGAGAAAGG CTCTCTTTT TTTTCTTTT TTTTGGCA GAGTGCTGCC TCCTAGAAAT TTCTCTGGT  
AACTTCCTTC TCTGAAGCAC AGATAAAGAA AACAATTACA GTAGAAACAT TTATGAGGGA CACATTGGAG GCCGATGAAG  
CTTTTCAAGT TCCAGCAGTG CAGGGATGTG GGCAGAACTG ACATTGGAAG ATACTAGAAT GATGGAATTT CAGTTGGAGA  
GGACTGCCCT TTTTAATGTC TGGGGAGTCT GCTCAGGGAG AAATGACAAG TCTGGCGGGG ACAAGTATGG GATTGTGTAA  
70 GACTTGGATC AACTTGGGAT ACAGGGTGGG GGTGGGAGT GGAATCAATG AATGATGCCA GAGCAGATCA ACTAACAAGA  
GGACCCTGAT GAGCCCCAGG CAGAGGCGTC TCCCTTATGC CCAACTCTGA AGTGTGTGT AGTAAACACC AGAACGCCAT  
TGTTGTACT GCTGAATTTT ATTTTGGGCT GTACATATT AGATGCTTAA GGTAAAAATG ATAAAGCCCT CAAGCCACTG  
TGTGGGTTTG GGTCAAAGTGT TTCTTCTTG CTGCTCTCT ACACAGCCCTG GTTAAAAATA TCCCTTTGGA TGGTCTGAG  
AAGCACTGA ACCAAGTGGG TCCCAAATA ACAATGGCGT GCAAGTGTCT GGTTCACAGA AGTTGGTGAC TAGGTAAAGCA  
75 GCTTCAGGGA GAGGGGGCTG ATTCCAGAC AGTCGCGCTG TCCTGCGGGG ATGGGGCTGA GGCTTGGGGA ATGTGGCAG



- GAGGATATGC CATTGATTC TGTGACAC GTTCTTTTCC CTTCTTTCTG TATGTCGGT CATTCTGCTA TTCTGTCGTT  
CCTCACATAG GTTGGACATT GGCCGGCTGC CAGCATAAGT GCCAGTGTGA TTTTGCTAGG TGTGAGCTGA GAAAGAGAGG  
TGGAGGCTAA GCAGGTGTGA TGCTTCTCAG AGGTGCTGAG TTTTGGCCCT TCTGAGCAGG GAATCTTTGC TTATCCCTTT  
5 GACCAAGGAT CTTTGCTGCA AAGGCTGGGT ATCGGCTGTG CTCAGCAAAG CGTCAACTCG TGCAAGAACT TAGCAGGAAT  
AGTCTGGCT AAGGTAGGA GGCTGCCACC AAAGTCTCTT TTTTGTCTCT CTGCTTCTCC CGTTTGCCCT CITATCATGA  
GATCTTTTTC CTAAGCTGGC AGAAAGATTG CATAGTCAGT GCTTCCAGCT CTGCTCCAC CTGATCTGCT ACTGTCTCT  
GGTCCCTGAA TGAATGAACT CTGATACCCA ATCTTGTCTC GAGCCTTCTC TATGCCACTC ATGGCTCCTC TTCTGTCTTT  
TCCATCTTTT TGCTGAGAGT TCTGAGCTCT GTACTTCTCT TGGGCCATC TCACITCTCT AAACACCCCT GAAGAGGGTT  
GCTTATCTTG ATGGAACCTA AAAAGCCAAA AAGCTGCAGG CAGAGGCGTT GAGGACATCT GTTTGGGGAA CTAAGAGCAG  
10 GACACTTTC AGATTACGTC CATATAGAGC TGTCTACAG CATTCTGGAA ACTTGAGGAT GTGCGGTGCA TAAAGGGGCT  
GGAAGTGACC CACCTGTGAT GAGCCCTTTC TAAGGAGAAG GGTTCCTAAG AGATCACCCC ACCAGAAAAG GGTAGGAATG  
AGCAAGTTGG GAATTTTAGA CTGTCACTGC ACATGGACCT CTGGGAAGAC GTCTGGCGAG GCTAGGCC ACTGGCCCTA  
CAGACGGATC CTTTACCCAC ACCTGTCCCT GTGGAGGTTT CCTGGGAAG GCAAGATGCC CAACAACAGC ACTGCTCTGT  
CATTGGCCAA TGTACCTAC TCACCATGG AAATTTTCAT TGGACTCTGC GCCATAGTGG GCAACGTGCT GGTCTATCTG  
15 GTGTCAAGC TGAACCCAG CCTGCAGACC ACCACCTTCT ATTCTATTGT CTCTCTAGCC TGCTGACA TTGCTGTTGG  
GGTGTGGT ATGCTTTGG CCATTGTGT CAGCCTGGG TCACAATCC ACTTCTACAG CTGCTTTTT ATGACTTGCC  
TACTCTTAT CTTTACCCAC CCTCCATCA TGTCTTGT GGCATCGCT GTGGACCGAT ACTTGCGGGT CAAGCTTACC  
GTCAGGTAGC CTGCGGCTG GGTGGGAC CAATTGAGGC AGCTGGGAAA TGAGGCTACA AGCCAGAGC-3' (FRAG. NO.: ) (SEQ  
ID NO:12484)
- 20 5'-GGGCAATTG TTAGTTATCC GCCGCCACCA AGACGCGGCA CGGCGCCTGG ACCGGAGGGG CCCCAGCGCG GCGCGAACTT  
TGGGCTCGGG CGAGTGGGTG GTGCTCCGCC CAGCCCGAGA CGGGCGGGCG CGCGGGCCAA TGGGTGCCG CTCTTGGCCG  
CGGGGGGCCC CGACCCGTGG GTCCCGGCCA CCAGCGCCCC AGCCCCGAGG CTCAGAAAGC GCAGGCGGAG GCGCGTCCG  
GGCGTATGG CCATGCCCGG CGGGTCTCAC GCGGCTGCC CTGCGCCGGC GCGCCTTCGG TAGGGGGCGC CCGGGGCCCA  
GCTGGCCCGG CCATGTGCT GGAGACACAG GACGCGTGT ACCTGGCGCT GGAGCTGGTC ATCGCCGCTG TTTCGGTGGC  
25 GGGCAACGTG CTGGTGTGG CCGCGGTGG CACGGCGAAC ACTCTGCAGA CGCCACCAA CTACTTCTG GTGTCCCTGG  
CTGCGGCCGA CGTGGCCGTG GGGCTCTTCG CCATCCCTT TGCCATCACC ATCAGCCTGG GCTTCTGCAC TGACTTCTAC  
GGCTGCCTCT TCCTCGCTG CTTCGTGCTG GTGCTCAGC AGAGCTCCAT CTTCAGCCTT CTGGCCGTGG CAGTCGACAG  
ATACCTGTCC ATCTGTGTC CGCTCAGGTA TAAAGTTTG GTACAGGGA CCCGAGCAA AGGGGTCACT GCTGTCTCT  
GGGTCTTGC CTTTGGCATC GGATTGACTC CATTCTGGG GTGGAACAGT AAAGACAGT CCACCAACAA CTGCACAGAA  
30 CCCTGGGATG GAACACGAA TGAAGAGTGC TGCTTGTGA AGTGTCTCT TGAGAATGTG GTCCCCATGA GCTACATGGT  
ATATTCAAT TTTCTGGGT GTGTTCTGCC CCACTGCTT ATAATGCTGG TGATCTACAT TAAGATCTTC CTGGTGGCCT  
GCAGGCAGCT TCAGCGCACT GAGCTGATGG ACCACTCGAG GACCACCCTC CAGCGGGAGA TCCATGCAGC CAAGTCACTG  
GCCATGATTG TGGGGATTTT TGCCCTGTGC TGGTTACCTG TGCATGCTGT TAACTGTGTC ACTCTTTTCC AGCCAGCTCA  
GGGTAACAA AAGCCCAAGT GGGCAATGAA TATGGCCATT CTTCTGTAC ATGCCAATTC AGTTGTCAAT CCATTTGTCT  
35 ATGCTTACCG GAACCGAGAC TTCCGCTACA CTTTACAAA AATTATCTCC AGGTATCTTC TCTGCCAAGC AGATGTCAAG  
AGTGGGAATG GTCAGGCTGG GGTACAGCCT GCTCTCGGTG TGGGCTATG ATCTAGGCTC TCGCTCTTC CAGGAGAAGA  
TACAAATCCA CAAGAAACAA AGAGGACACG GCTGGTTTTT ATTGTGAAAG ATAGCTACAC CTCACAAGGA AATGGACTGC  
CTCTCTGAG CACTTCCCTG GAGTACCAC GTATCTAGT AATATGTATG TGTCAGTAGT AGGCTCCAAG GATTGACAAA  
TATATTATG ATCTATTCAG CTGCTTTTAC TGTGTGGATT ATGCCAACAG CTGGAATGGA TTCTAACAGA CTCCTTTGTT  
40 TTTAAAAGTC TGCCTGTGT ATGTGGAAA ATTACTGAAA CTATTTTACT GTGAAACAGT GTGAACATAT ATAATGCAAA  
TACTTTTTAA CTTAGAGGCA ATGAAAAAT AAAAGTTGAC TGTACTAAAA ATG-3' (FRAG. NO.: ) (SEQ ID NO:11794)
- 5'-GBG CB TGC-3' (FRAG. NO:1676) (SEQ ID NO:11060)  
5'-TTG TTG GGC-3' (FRAG. NO:1677) (SEQ ID NO:11061)  
5'-TGC CTT CCC BGG G-3' (FRAG. NO:1678) (SEQ ID NO:11062)
- 45 5'-GTT GTT GGG CAT CTT GCC-3' (FRAG. NO:1679) (SEQ ID NO:9372)  
5'-GTG GGC CTA GCT CTC GCC-3' (FRAG. NO:1680) (SEQ ID NO:9374)  
5'-ACA GAG CA TGC TGT TGT TGG GCA TCT TGC CTT CCC AGG G-3' (FRAG 982) (SEQ ID NO:10361)  
5'-BCB GBG CB TGC TGT TGT TGG GCB TCT TGC CTT CCC BGG G-3' (FRAG 983) (SEQ ID NO:10362)  
5'-CCC TTT TCT GGT GGG GTG-3' (FRAG 984) (SEQ ID NO:10363)  
50 5'-GTG CTG TTG TTG GGC-3' (FRAG 985) (SEQ ID NO:10364)  
5'-TTT CTT CTG TTC CC-3' (FRAG 986) (SEQ ID NO:10365)  
5'-CCC TTT TCT GGT GGG GTG-3' (FRAG 987) (SEQ ID NO:10366)  
5'-GTG CTG TTG TTG GGC-3' (FRAG 988) (SEQ ID NO:10367)  
5'-TTT CTT CTG TTC CC-3' (FRAG 989) (SEQ ID NO:10368)
- 55 **Human IgE Receptor (Nucleic Acid and Antisense Oligonucleotide Fragments)**  
5'-TTT CCC CTG GGT CTT CC CTC CTG CTC TTT TTT C ATT TGC TCT CCT ATT ACT TTC TGT GTC CAT TTT TTC ATT AAC CGA  
GCT GT BTT TGC TCT CCT BTT BCT TTC TGT GTC CBT TTT TTC BTT BBC CGB GCT GT-3' (FRAG. NO:1681) (SEQ ID NO:11063)  
5'-CCC CTG GG-3' (FRAG. NO:1682) (SEQ ID NO:11064)  
5'-GCTCTCCTBTT-3' (FRAG. NO:1683) (SEQ ID NO:11065)  
5'-CBTTBCCBGCTG-3' (FRAG. NO:1684) (SEQ ID NO:11066)  
60 5'-TTT CCC CTG GGT CTT CC-3' (FRAG 990) (SEQ ID NO:10369)  
5'-CTC CTG CTC TTT TTT C-3' (FRAG 991) (SEQ ID NO:10370)  
ATTTGCTCTCCTATTACTTCTGTGTCCATTTTTCATTAAACCGAGCTGT (FRAG 992) (SEQ ID NO:10371)  
BTTTGTCTCCTBTTBCTTTCTGTGTCCBTTTTCBTTBCCGBGCTGT (FRAG 993) (SEQ ID NO:10372)
- 65 **Human Fc- (Receptor CD23 Antigen (IgE Receptor))**  
Nucleic Acid and Antisense Oligonucleotide Fragments  
5'-GCC TGT GTC TGT CCT CCT GCT TCG TTC CTC CTG CTT GGT GCC CTT GCC G GTC CTG CTC CTC CGG GCT GTG G  
GTC GTG GCC CTG GCT CCG GCT GGT GGG CTC CCC TGG CCT TCG CTG GCT GGC GGC GTG C GGG TCT TGC TCT GGG CCT  
GGC TGT GGC CGT GGT TGG GGG TCT TC GCT GCC TCC GTT TGG GTG GC TCT CTG AAT ATT GAC CTT CCT CCA TGG CGG  
70 TCC TGC TTG GAT TCT CCC GA TCT CTG BBT BTT GBC CTT CCT CCB TGG CGG TCC TGC TTG GBT TCT CCC GB-3' (FRAG  
1685) (SEQ ID NO:11067)  
5'-GT CCT CCT-3' (FRAG 1686) (SEQ ID NO:11068)  
5'-TGT GTC TGT CCT CC-3' (FRAG 1687) (SEQ ID NO:11069)  
5'-GTG GCC CTG GC-3' (FRAG 1688) (SEQ ID NO:11070)

- 5'-CGT GGT TGG GG-3' (FRAG 1689) (SEQ ID NO:11071)  
 5'-TCT CTG BBT BTT GBC C-3' (FRAG 1690) (SEQ ID NO:11072)  
 5'-GCC TGT GTC TGT CCT CCT-3' (FRAG 994) (SEQ ID NO:10373)  
 5'-GCT TCG TTC CTC TCG TTC-3' (FRAG 995) (SEQ ID NO:10374)  
 5'-CTG CTT GGT GCC CTT GCC G-3' (FRAG 996) (SEQ ID NO:10375)  
 5'-GTC CTG CTC CTC CGG GCT GTG G-3' (FRAG 997) (SEQ ID NO:10376)  
 5'-GTC GTG GCC CTG GCT CCG GCT GGT GGG CTC CCC TGG-3' (FRAG 998) (SEQ ID NO:10377)  
 5'-CCT TCG CTG GCT GGC GGC GTG C-3' (FRAG 999) (SEQ ID NO:10378)  
 5'-GGG TCT TGC TCT GGG CCT GGC TGT-3' (FRAG 1000) (SEQ ID NO:10379)  
 5'-GGC CGT GGT TGG GGG TCT TC-3' (FRAG 1001) (SEQ ID NO:10380)  
 5'-GCT GCC TCC GTT TGG GTG GC (FRAG 1002) (SEQ ID NO:10381)  
 5'-TCT CTG AAT ATT GAC CTT CCT CCA TGG CGG TCC TGC TTG GAT TCT CCC GA (FRAG 1003) (SEQ ID NO:10382)  
 5'-TCT CTG BBT BTT GBC CTT CCT CCB TGG CGG TCC TGC TTG GBT TCT CCC GB (FRAG 1004) (SEQ ID NO:10383)
- Human IgE Receptor ( Subunit Nucleic Acid and Antisense Oligonucleotide Fragments**
- 5'-GCC TTT CCT GGT TCT CTT GTT TTT GGG GTT TGG CTT ACA GTA GAG TAG GGG ATT CCA TGG CAG GAG CCA TCT TCT TCA TGG ACT CC TTC AAG GAG ACC TTA GGT TTC TGA GGG ACT GCT AAC ACG CCA TCT GGA GC BCB GTB GBG TBG GGG BTT CCB TGG CBG GBG CCB TCT TCB TGG BCT CC TTC BBG GBG BCC TTB GGT TTC TGB GGG BCT GCT BBC BCG CCB TCT GGB GC-3' (FRAG. NO: 1691) (SEQ ID NO:11073)  
 5'-TGG BCT CC -3' (FRAG. NO: 1692) (SEQ ID NO:11074)  
 5'-CCB TCT GGB-3' (FRAG. NO: 1693) (SEQ ID NO:11075)  
 5'-CT GCT BBC BCG-3' (FRAG. NO: 1694) (SEQ ID NO:11076)  
 5'-GTT TTT GGG GTT TG-3' (FRAG. NO: 1695) (SEQ ID NO:11077)  
 5'-GCC TTT CCT GGT TCT CTT GTT TTT GGG GTT TGG CTT-3' (FRAG. NO:1005) (SEQ ID NO:10384)  
 5'-ACAGTAGAGTAGGGGATTCCATGGCAGGAGCCATCTTCTTCATGGACTCC-3'(FRAG.NO:1006)(SEQ ID NO:10385)  
 5'-TTC AAG GAG ACC TTA GGT TTC TGA GGG ACT GCT AAC ACG CCA TCT GGA GC-3' (FRAG. NO:1007) (SEQ ID NO:10386)  
 5'-BCB GTB GBG TBG GGG BTT CCB TGG CBG GBG CCB TCT TCT TCB TGG BCT CC TTC BBG GBG BCC TTB GGT TTC TGB GGG-3' (FRAG. NO:1008) (SEQ ID NO:10387)  
 5'-BCT GCT BBC BCG CCB TCT GGB GC-3' (FRAG. NO:1009) (SEQ ID NO:10388)  
 5'-GTT GTT TTT GGG GTT TGG CTT-3' (FRAG. NO:1010) (SEQ ID NO:10389)  
 5'-GCC TTT CCT GGT TCT CTT-3' (FRAG. NO:1011) (SEQ ID NO:10390)  
 5'-BCBGTBGBGTBGGGGBTTCBTTGGCBGGGCBCTCTTCTTCTGGBCTCC-3'(FRAG.NO:1012) (SEQ ID NO:10391)  
 5'-TTC BBG GBG BCC TTB GGT TTC TGB GGG BCT GCT BBC BCG CCB TCT GGB GC-3' (FRAG.NO:1013) (SEQ ID NO:10392)
- Human IgE Receptor (Fc Epsilon R) Nucleic Acid and Antisense Oligonucleotide Fragments**
- 5'-GCC TGT GTC TGT CCT GCT TCG TTC CTC TCG TTC CTG CTT GGT GCC CTT GCC G GTC CTC CTC CGG GCT GTG G GTC CTC GCC CTG GCT CCG GCT GGT GGG CTC CCC TGG CCT TCG CTG GCT GGC GGC GTG C CCC BGB BCG BGB CCC GGB CCG BCB GGC CGT GGT TGG GGG TCT TC GCT GCC TCC GTT TGG GTG GC GAT CTC TGA ATA TTGA CCT TCC ATG GCG GTC CTG CTT GGA GBT CTC TGB BTB TTGB CCT TCC BTG GCG GTC CTG CTT GGB-3' (FRAG: 1696) (SEQ ID NO:11078)  
 5'-GCC TTT CCT GGT TCT CTT-3' (FRAG: 1697) (SEQ ID NO:12370)  
 5'-BGB BCG BGB C-3' (FRAG: 1698) (SEQ ID NO:11080)  
 5'-TGB BTB TTGB-3' (FRAG: 1699) (SEQ ID NO:11081)  
 5'-GCC TGT GTC TGT CCT CCT-3' (FRAG. NO:1014) (SEQ ID NO:10393)  
 5'-GCT TCG TTC CTC TCG TTC-3' (FRAG. NO:1015)(SEQ ID NO:10394)  
 5'-CTG CTT GGT GCC CTT GCC G-3' (FRAG. NO:1016)(SEQ ID NO:10395)  
 5'-GTC CTG CTC CTC CGG GCT GTG G-3' (FRAG. NO:1017)(SEQ ID NO:10396)  
 5'-GTC CTC GCC CTG GCT CCG GCT GGT GGG CTC CCC TGG-3' (FRAG. NO:1018) (SEQ ID NO:10397)  
 5'-CCT TCG CTG GCT GGC GGC GTG C-3' (FRAG. NO:1019) (SEQ ID NO:10398)  
 5'-CCC BGB BCG BGB CCC GGB CCG BCB-3' (FRAG. NO:1020) (SEQ ID NO:10399)  
 5'-GGC CGT GGT TGG GGG TCT TC-3' (FRAG. NO:1021) (SEQ ID NO:10400)  
 5'-GCT GCC TCC GTT TGG GTG GC-3' (FRAG. NO:1022) (SEQ ID NO:10401)  
 5'-GBT CTC TGB BTB TTGB CCT TCC BTG GCG GTC CTG CTT GGB-3' (FRAG. NO:1023) (SEQ ID NO:10402)
- Human High Affinity IgE Receptor Oligonucleotide Fragments**
- 5'-AACAAAGAAAA GCGTTGGTAG CTCTGGTGAA TCCCAAAAGA ATGTGGCAGT TGCTAGCCAT GCTCCTGAAT ATGTATAAAC AGTACATCAT ATGACTAAGA GTTTGACTTA GGGGTTAGT TTTATGTGTT TGAACCCCAA ATTAGTTATT TAATAGTTGG CACCCCAAAA CAAGTTACTT AACCTCACTA AGGTTCACTT TTCCTGTTTA TAAATGTAG ATAGTGATAG TATGTACTTT ATAGGATTAT TGTGAAAAAT AAATGAAATA TCAGATTTAT TTAGGATAAC ACCTGGCATA TGTTTGGTAT TCAGAATTAG TTGCTGCTGT TTAATCTGCT TCTCCCTTGC ATCCCACTTT TCTAAGTTGT AAATAAATA GTTGACACA GATTGACAGA TTAAGAAAGG CTTGTGATTG TGCTAGACCT ATGCCTATGC CTCTGTCTCA CCAGATTCCA GGTGTATATG TGGAGGTGGG ATAGGGAGTG GAGTAAGTGG GTAAATATTA AATTGCCAG TTGGGCACCA TCCTGAATAT TATCTCTAAA GAAAGAAAGCA AAACCAGGCA CAGCTGATGG GTTAACCAGA TATGATACAG AAAACATTTT CTCTGCTTTT TTGGTTTAAA GCCTATATTT GAAGCCTTAG ATCTCTCCAG CACAGTAAGC ACCAGGAGTC CATGAAGAAG ATG GATCTTCATG TGGAAATGACT GGTTTCATTC AATAGACTTA ATTCAGCAGT CTGTGGGGAA GAGCAAGGTA TGATAGAATG GTTCCTCAAG TGCTTCAGAT GTGAAGTGGG TTAAATATA CTGTCCCTGT CTCTTCAGA GTTTTGGTAA AGATAAAATA GGACACTCAT TTAAGGACAA TCTTTGCAAA TTGACCTAGA GCAAAAAAAC AGAAGAATTA GTAAAGGAAT CCTGGAGAAA GCCCCTGCTG TGTATTTAAA GGAGAAAGGG AGATCATGTT GGGAAATTA AATATTAAAA GTAAACAAAA GCTAGGAAGT AAAATAAAAT AAATTATATG GCCTAGATCC CCATAAGTAA TGGTTTAACT TCTGCCCTCC TGTGTCTGA GCCAGATTAG GGCACAGTAG AGAAAGAGGA GTCTCTGAAA ATGTTTCCAA TTTCCGTGGT CAGACAGCGG ATCATCAGTA AATCAGATGA AAATTTGTGG ATTTATGCAC TAACTGATCA GCAGGAAATT AAACAAGAAA AGCGTTGGTA GCTCTGGTGA ATCCCAAAAG AATTTGGCAG TTGCTAGCCA TGCTCCTGAA TATGTATAAA CAGTACATCA TATGACTAAG AGTTTGACTT AGGGGTTAGA TTTTATGTGT TTGAACCCCA AATTATGTTAT TTAATAGTTG GCACCCCAAA ACAAGTTACT TAACCTCACT AAGATTCACT TTTCCTGTTT ATAAAAATGA GATAGTGATA GTATGTACTT TATAGGATTA TTGTGAAAAA TAAATGAAAT ATCAGATTTA TTTAGGATAA CACCTGGCAT ATGTTTGGTA TTCAGTAATT AGTGTCTGCT GTTTTATTCT GCTCTCCCTT GCATCCCACT TTTCTAAGTT GTAAACTAAA TAGTTGTACA

CAGATTGACA GATTAAGAAA GGCTTGTGAT TGTGCTAGAC CTATGCCTCT CTCTCACCAG ATTCCAGGTG TATATGTGGA  
 GGTGGGATAG GGAGTGGAGT AAGTGGGTAA ATATTAATTT GCCCAGTTGG GCACCATCCT GAATATTATC TCTAAAGAAA  
 GAAGCAAAAC CAGGCACAGC TGATGGGTTA ACCAGATATG ATACAGAAAA CATTTCTTTC TGCTTTTGGG TTTTAAAGCCT  
 5 ATATTTGAAG CCTTAGATCT CTCCAGCACA GTAAGCACCAGGAGTCCATG AAGAAGATGG CTCCTGCCAT GGAATCCCTT  
 ACTCTACTGT GTGTAGCCTT ACTGTTCTTC GGTAAAGTAGA GATTCAATTA CCCCTCCCAG GGAGGCCCAA ATGAATTGGG  
 GGAGCAGCTG GGGTAGGAAC CTTACTGTG GTGGTGAAGT TTTTCTAGGA CATGTGCAAA CTATTGGGCA TTTCCAGGG  
 ACTCTGTAGT GGAGCCAAGC TAGAAAGCAG AGGCAAGTGG GCTGAGCAAC ACCTAAGGAG GAAGCCAGAG TGAAAGCTTG  
 GTTCCTTGCA TTGCTCTGG CATCTTCCAG AGTGCAAAT TCCTACCAAG GTAATGAGGG TAGAGGAGAG AAAGAAGCTC  
 10 TTTCTTCCCC TGATTCTCAT TCCTGAAAAG ACGGTTGGTC CTTAAAATTC CATGGATGTA GATCTTATCC CCACACCCAG  
 ATTCTAGTCC TCTGGAGATA AAGAAGACTG CTGGACACTA ATGTATCCTC TCTGGACTTT TGCAGCTCCA GATGGCGTGT  
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 CCCATCACTT CTGCTTTCTA ATGAGCATGA ATCTGTTCCT TGGCCAGACT ACTTTCCCTC TCCACCTTGC TTTGTCTTTC  
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 15 CATGTCTCAT TCCTCTCCT AGACACTTTC GCATATCTC GCTCAATAAT TACATTATTA TTATTATGTC CATTTTATAA  
 TTGAGGATGC TGAAACTCAG TGATTTTCTG GTGGTTACAT GGCTAAGGAA CTGGATTTC ACCTAAGTTC CTGGATCTA  
 AGTCCAGTTC TCTTCTGACT ATATCACCTT TTTGTATCA CCATGTATCT ACTTCTTTGG TCTCTGTTCA AATTTGCAT  
 ACATCCCTCT GTTCCAGGAA GCCATTCAAG ACTGACTTTC TTAGTGCTC TCACTACTTT TCAGAACTGA CATATGTTT  
 TCACTCTGTA TATACTTACA ATTAATAGT CATAAATAT CAGAGCTGG AGAAACCTTA TATTTTATCC AGTCCAGTAA  
 ATTTATCCAT CCATAATTCA CTCATTCAAT CACATAATAA ATATTTAATG TAACAATGGT TGAACATGGC AGACAGGTTC  
 20 TCTACCTCAA AAGAGATTGC AGTCTCAT TACAGATCT GAATGAAAT TAACAGAAGT AGAGTGAGTC AGCTCAAAATC  
 ACATAGTGAA TTGGTTTCTT TGTTTTAA TCTCTGCTAT ATGTGTCTG TCTTTCTCCC TGTGTGGGG GTTCCCTGGG  
 GCACCAATAC TAATTTCTCC TTCCCTTAGA AATCAAAACA GGGTCTTATC ACCAACAGAA TAAGGACAGG TTGACCACTG  
 ATTTGTCAGAA TATTGCTTCG TTTGTACTTT TAAGCTTAGA CAGTTTTCAA TGACTTTTTT TCTCTCTACA TGTCTTTTCA  
 TATTTTATC TTCTTGAAGT CCTCAGAAA CCTAAGTCT CCTTGAACCC TCCATGGAAT AGAATATTTA AAGGAGAGAA  
 25 TGTGACTCTT ACATGTAATG GGAACAATTT CTTTGAAGTC AGTTCACCA AATGGTTCCA CAATGGCAGC CTTTCAAGAG  
 AGACAAATTC AAGTTTGAAT ATTGTGAATG CCAAATTTGA AGACAGTGGG GAATACAAAT GTCAGACCA ACAAGTTAAT  
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 40 CAACAAAAAG TTCTTTTAC AATTAAACGGT GGTGTAACAA TTTAGCCAC AGTTTTATCC CATGAGAAAC CAGAAATCTAA  
 TACAAGTTAA ATGACTTGGC TAAGGGCCAC TTGACTAATA GTAATTGAAC CTAAACTTTC AGAATCCAAC TCCAGGAACA  
 TACTCTAGC ACTATTATC AATAAAGTTA TATGATAAAT ACATACAAT TTATCTGTCA ACTAAAAATA ACAACAGAGG  
 CTGGGCATGG TGGCTACAC CCGTAATCCC AGCATTTTGG CAGGCTGAGG CAGGTGGATC ACCTGAGGTC AGGAGTTTGA  
 GACCAGCTG ACCAACATGG TGAACCTCA TCTCTACTAA ATATAAAAAA TTAGCTGAGT GTGATAGTGC ATACCTGTAA  
 45 TCCAGTACT TAAGAGGCTG AGGCAGGAGG CTGTGTTGAA CCTGGAAGGC AGAGGTTGCA GTGAGCTGAG ATTGTGCCAT  
 TGCACCTAC CCTGGGCAAT AAGTGCGAAT TCTGTCTCAA AATAATAATA ATAATAATAG AAAATAAAGT TGTCTCTATG  
 AAAAAATGAG AAAGAGATTG CTGGGGTGAG AAACATTAAG ATCAATGGGC ATATGGTGAC CTCTATGCC CTAGAACTC  
 TTTTANGGTA TTTTCTCTCT GTATCTCTTT TACNCTCGT TCTATCTGGA AAAATAGGTG GATGAGTGA ATAAATACGG  
 TATATACTTT TAAAGGTCT AATTGACATA TATAAATGGC AAGTATTICA GATGTCAATT TGCTAACCTT GACACACATA  
 50 GACACACATG AAAACATCAC CACATTAATA CAATGTATGT ATCCATCATT CCAAAAGCTT CCCTGTGTAT CTTTGTAACT  
 CTCTCTCTCT CCCCCTACTC CTGTCTCTCT CGTTCCCAAG AAAACATTGA TCTGCTTCT GTGAATATAA ATTAACCTAC  
 ATTTTITAGA GCTTTATATA AGTATGTCT CTTTACTGTT TGTCTTCTT CGCTGCACAG TTATTTTGA ATTTCTCAAG  
 TTTTCTTAT ATATCGATAC TTCAATCACA AGAATATATT TTAATTCTAG ACTATGTAC ATTGACTTTG TCGTCTGCTA  
 AATCCCTAGT GCTCAGATGA CTGTTCAGG ACTCTCTCT AACCTGTACC TCTGTTANAT TGAAACTTGT CTCTACTGTC  
 TTTTATTTT AAACACAGCT TATTAGGTGT CTCTCAACCC ATCAAACNCA CAATCTGAGT CTTTAGGAGA TTGCTTTGAA  
 55 TTTGTGCTAT TGACTTATAT NTATATNAAA TNGTAAATG TTTGGTAAAA ATATCATCAT GTACNTTITC ATAATTACGC  
 TATNTNCACA TGATATATGT CAGACTCTGG AAATATGCAT GCCACAGACA CGTGTTTCTT GCCTAAAGGG GCTGATGGAA  
 GACNCACATA CNAATAGAGC ATTGCAGTAG AATGAGAGTG GTGGTCTAAN CAGTACATGT CCTGATGTTG CTCGGACAGT  
 TACTACNCCA AGAGTACCCC CTGCATTGTC AGGGTTAGCA TCTCTGGGAA GCCTCATGTA AATGAAGAA TTTGATGCTC  
 60 ATCCAGGACC TAATGAATAA GAATCTGCAT TTAGCAAGA CCCTCATATG ATTCATATAC ACTTTTTTTT TTTTTTTT  
 GATGGAGTCT CACTCTTGTG GCCCAGGCTG GAGTGCAATG GCATGATCTT GGCTCACTGC AACCTCTGCC TCCCGGGTTC  
 AAGTGATTCT CCGTCTCTAG CCTCCCTAGT AGCTGGGACT ACAGGTGCAT GCCACAGTGG CTGGCTAATT TTTGATTTT  
 TAGTAGAGAC AGGGTTTCAC CATTTTGGTC AGGCTGTCT TGAACCTATG ACCTCCGGTG ATTCCCCCGC CTCGGCTTCC  
 CAAAGTGCTG GGATACAGA CATGAGCCAC CACACCCGCC TTATTCGTAT ACNCAATTTA TTCTGAGAAG CACTCTATAG  
 65 AAAATAAGAA TAAGAAAAATA TTGGGCTCAC AGGTGACATT AATAAGTAAC TTTATCGAGT ACCCAAAT TTACCTATGT  
 TTGGAAGATG GGGTTAAAAG GACACATTGA AAACAAGAAC TCATTGTGGC TTTTITTTCC TCCTTTTGA ACAGTTTCT  
 ATTTCTGAAA TGTGTCAAT TATATCTGAA AGGAGAAATG CAACATATCT GGTGAGTTGC CCGTTTCTGT CTTTGTCCAT  
 CCTGAAAAG ATAGAAAGAA CAGAGTTTAA AGAGTCTTAA GGAACACACA TCTTTGTCT CTATATTACT TGTGAATGTG  
 GATATATGAT TTTGTTTCAA TCTATTTTGT GTCCTAAGGC TTTTGTCAAC AGAAGTTGGA TATATCATTA GAAACATAAA  
 70 TTGTACCAT TAACATACAT GAAGTTTATG TTTACCTTGA CGTTCTTCTA AAAAGTGTCC TACACCGGCA TTGCTCTTGT  
 AGGCATATTC ACATGATCAA ATAAATAAT TAGTTTCTAA TTAAGAGAA TATTTGAGGA AAGACCGTAC GTGTCTATGT  
 GGTCTCTGAA GGCAGTCCAG TGAGAAAGTA ATATATGCTT CATTAACCAA TGCGGACATT TTCAGGGTTT CCCITTTTAA  
 CCAAAATTTG GAAGCAATGT GGAATTTACT GGATGCATCC AGCCCTGAAA TGAAGATAGG TTTATTTAAT GTCCAGCAA  
 GTCCAGGCC AGGTCTGAGT GTTCTTCAAT ATTATCAGT GAGAGGAAG CTGGGAGCAA ACACCTGCCAG CAGCATAGCT  
 75 GGGGGAACGG GAATTACCAT CCTGATCATC AACCTGAAGA AGAGCTTGGC CTATATCCAC ATCCACAGTT GCCAGAAAT  
 TTTTGAGACC AAGTGCTTTA TGGCTTCTT TTCCACTGTA TGTATTTTT TTTGTGTGGG AAGACTAAGA TTCTGGGTCC

5 TAATGTAAGT AAGAAGCCCT CTTCTCCTGT TCCATGAACA CCATCCTTTT CTGTAACCTC TATTACACAG TATAGTGGTT  
 CTGTAAGTTC ACACAGCCCA GGGAGATGCT GGCTGCCAC TCCCTCAAC CCAGGCAAAAT TCCTCGGGGT TAAAGTTATC  
 TACTGCAAGT GACGATCTCT GGGTTTTTCT GTGCCTGTGT TTGTGTGTGT GTGTGTGTGT GTGTGTGTGT GTATGTGTCA  
 CTTTAAAGG ACTGGTCAGA TGGTAGGGAG ATGAAACAGG GAGATGCTAT AAGAAAAATA ACTTTTGGGG CGAATACCAA  
 TGTGACTCTT TTTGTTTGTG ATTTGTGTCT GTTCAATAGG AATTTGTAGT GATGATGCTG TTTCTCACCA TTCTGGGACT  
 TGGTAGTGCT GTGTCACTCA CAATCTGTGG AGCTGGGGAA GAACTCAAA GAAACAAGGT AGATAGAAGC CCGATATAAA  
 ATCTTGAATG ACAGGTTAAC GAATTTGGAGC TTTATTCCTT AAAATATGGC CTGGGTTTTT TGAACATTT CTTCAGAAA  
 ATAGTTTCTC CAAGTTTTAT TACTTTGGTT TACAAATCTC ACATTTAAAT CACATTTTAT ACCATAAGTA GCACACATTT  
 10 CATAATATTC CTCTGAATGA GGGTTGGGAT AATAGGACTG ATATGTTAGA AATGCCTTAA AGTGTGTGGA GCATGAGAGA  
 TGGATGTACA GAAGGCTTGT GAGGAAACCA CCCAGGTATC TGGCCTTGT TTTGCCCCA GAACTAGCCG CCTATTCTGT  
 TTTCTGTTTT ATTCTTTTGT TTCTTGACTT TTCCTTTCCA ACTTGCTCTA AAACCTCAGT TTTCTTTCTT TTTGATTTCA  
 TGAATACCAA ATGTTTTTAC TTGCCTCACC CGTCCATTAC ACCTTTGATA AGAACCACCA GACCTTGTGC TCATGTACTT  
 GCCCATGTCT GATGGAAGAA ACATACTCTC TCCATCTGTG CACITTCCTG AGGCATTCAA GTCTAGCCAC CTTTAAAAAT  
 15 CACTCTCCTC CAGGCTGGGC ACGGTGTAC GCTCTGAATC TCAGCACTTT GTGAGGCTGA GGAGGGCGGA TCACCTGAAG  
 TCAGGAGTTC AAAACAGCC TGGCCAAATG GCAAAACCAA ATCTTCTTCA ATTATAACCA AATCTTAAAC CAAATCTCTA  
 CTAATAAATA CAACAACAAAC AAACAACAAAC AAAAAAAGAA CAATAGCCCA GCGTGGTGGC AGGTACCTGA  
 GGTTCCAGAT ACTTGGGAGG CTGAAGCAGG AGAATCGCTT GAGCCCAAGA GATGGAGGTT GCAGTGAGCC GCATCATTCG  
 CACTGCACCA CAGCCAGGGT GACAGAGCCA TACTTCCAG CACATTGGGA GGCCAAAGCT GAAGAATAAT TTGAGGTGAG  
 TTTTGGGAGA CCAGCTGGC CAACATGGTG AAACCTCGTC TGTACTAAAA ATATAAAACT TAGTGGGGCA TGGGGGCACA  
 20 CACTGTAAAT TTCAGCTGT TAGGAGGCTG AGGCAGGAGA ATTGCTTGAA CCCGGGAGGG GGAAGTTGCA GGAAGCCAAAG  
 ATCGTGGCCA CTGCACTCCA GCCTGGGTGA CATAGTGAGA TTCTGTCTCA AAAAAAATAA AAGAAATTTA AAAAATCACT  
 CTCTTCCAAA GATAGATAAA TAAGACAGCA GATATACTAA GGAATAACCT CACCAACTTG TCATTGACTG ACATGATTTT  
 TTTTGGCCCA CTGGCCAGC TAGTCTGGTT TGGTTTTCTG GAAATGAAAG AAATAATCAG AGTTTAATGA CAGAGCCGCT  
 GAGACCCAGA AAGACAAAAG TAGATGAGGT AAGTCTCTTG AGCGAGACTT CTAGGGATGG GAAATTTGTG GTGATTGATA  
 25 TGAATGATT TTTCCCTTAT CAGGTTCCAG AGGATCGTGT TTATGAAGAA TTAACATAT ATTCACTAC TTACAGTGAG  
 TTGGAAGACC CAGGGGAAAT GTCTCCTCCC ATTGATTTAT AAGAATCAGG TGTCAGAAC ACTCTGATC ACAGCCAAAG  
 ATCCGAAAGG CCAAGGTTTT GTTAAGGGGC TACTGGAATA ATTCTATTCT TCTCCACAGC CTGCTGGTTT TACATTAGAT  
 TTATTCCGCT GATAAGAATA TTTTGTCTCT GCTGCTCTG TCCACCTTAA TATGCTCCTT CTATTGTAG ATATGATAGA  
 CTCCTATTTT TCTTGTTTTA TATTATGACC ACACACATCT CTGCTGGAAG GTCAACATGT AGTAAGCAAG ATTTAATCTG  
 30 TTGATTATAA CTGTGCAAAAT ACAGAAAAAA AGAAGGCTGG CTGAAAGTGG AGTTAAACTT TGACAGTTTG ATAATATTG  
 GTTCTTAGGG TTTTTTTTTT TTTTAGCATT CTTAATAGTT ACAGTTGGGC ATGATTGTGA CCATCCACCC ATACCCACAC  
 AGTCACAGTC ACACACACAT ATGTATTACT TACACTATAT ATAACCTTCT ATGCAAAAT TTTACCACCA GTCAATAATA  
 CATTTTTGCC AAGACATGAA GTTTTATAAA GATCTGTATA ATTGCCTGAA TCACCAGCAC ATTCAGTGAC ATGATATTAT  
 TGCAGATTG ACAAGTAGGA AGTGGGGAAC TTTTATTAAG TTACTCGTTG TCTGGGGAGG TAAATAGGTT AAAACAGGG  
 35 AAATTATAAG TGCAGAGATT AACATTTTAC AAATGTTTAG TGAACACATT GTGAAAAAAG AAGACTAAAT TAAGACCTGA  
 GCTGAAATAA AGTAGCTGG AAATGGAAAT AATGGTTATA TCTAAAACAT GTAGAAAAAG AGTAACTGGT AAGTCTTTGT  
 AAAAAATTAA AGAATAAAGT TAGACAAGCA ACTGGTTGAC TAATACATTA AGCGTTTGAG TCTAAGATGA AAGGAGAACA  
 TGGTATTATG TGATAGAAAT ATAAAAAGGG TCGGGGCGGG AGGCTCACGC CTGTAATCCC AGCCCTTTGG GAGGCCGAGG  
 40 TGGCAGATC ACGAAGTCAG TAGTTTGAGA CAGCCGTGGC CAACATAGTG AAACCCCGTC TCTACTAAAA ATACAAAAAA  
 AAAATTAGCT GGGTGTGGTG GCAGTCACCT GTAGTCCAG CTACTTGGGA GGATGAGGCA GGAGAATCGC TTGAACCTGG  
 GAGGCGGAGG TTGCAGTGAG CCGAGATCGC ACCAGTGAC TCCAGCCCTG GTGACAATGG GAGACTCCAT CTCAAAAAAA  
 AAAAAAATAA AAAAAAGATA AAAAGTCAGA AATCTGAAAA TGGGAGGAAG AGTACAAATA GACCTAAAT AAGTCTCATT  
 TTTTGGCTTT GATTTTGGGG AGACAAAGGG AAATGCAGCC ATAGAGGGCC TGATGACATC CAATACATGA GTTCTGGTAA  
 AGATAAAATT TGATACACGG TTTGGTGTCA TTATAAGAGA AACTATTATT AAATGAAGCA AGTTAACTCT CTAAGAGAAAT  
 45 TATTTTGAGA TAGAAGTCAA GCTAAGCTAA ACTTGCAATG CCTATAATTG GAGGGAATAA CTAAGGATAA AACTTAGCCT  
 AGAAGATACA ATAATTAGTC ATAAACATGC ATTGTGAAAC TGTAGAGAGC AGGTAGCCCA AAATAGAGAA AGATTAGATA  
 AAGAGAAAAA AAGTATCCAT CAGAGACAGT ATCTCTAGGC TGTGGCAAGA GAAAAAGTCCA CAGTGATAAG CAACCTCCAT  
 TAAGGCATGA ATATGGGCCA GAGAAAAACG CAATAGTCAA TGAATGCAAA AGGTGCTGAG CAAATTCCAC ACATGAGTAC  
 TGTGCATGAG TAAATGAATA AAACATTTGC AAAGACCTTT AGAGAAAGAG AATGGGAGCA TATGTGCGAA ATAAGATAGT  
 50 TGATTATGAA TAGAAGGTAG TGAAGAAAAAG CAAGCTAAGA AAAAAATCTG TTTATAAAG AAGGAAAGAA TAGTTTATGT  
 TTTTAGCCTA AGTATAAGAG TCCTACAGAT GGACTGAAAA AAATCAGTCT GAGAGTATTA GTCACAATTA ATGAATAAT  
 TACATTTTAT GTATTGAGGA TGCCAAGATT AAAAGGTGAC AGGTAGATGT TAATTTCCCT AGATTGTGAA AGTGATCAGC  
 ACAATCACAC AACAAATAAT TAAGTGACTT GGTATGCTTT ATTTAATTGT AGGGCCTGAG GTTTTCCATT CTCAITTTTC  
 TAAAAACAA TTTTGTCTCT CCAAAATTGA CAGCAGAATA AAAACCTTAC CCTTTCATG TGTATCATG TAAGCTGCAT  
 55 TCTACTCTT GATCATCTGT AGGTATTAAT CACATCATCT CCATGGCATG GATGTTTACA TACAGACTCT TAACCTGGT  
 TTACCAGGAC CTCTAGGAGT GGATCCAATC TATATCTTTA CAGTTGTATA GTATATGATA TCTCTTTTAT TTCACTCAAT  
 TTATATTTTC ATCAITGACT ACATATTTCT TATACACAAC ACACAATTTA TGAATTTTTT CTCAAGATCA TTCTGAGAGT  
 TGCCCCACCC TACCTGCCTT TTATAGTACG CCCACCTCAG GCAGACACAG AGCACAATGC TGGGGTTCTC TTCACACTAT  
 CACTGCCCA AATTGTCTTT CTAAATTTCA ACTTCAATGT CATCTTCTCC ATGAAGACCA CTGAATGAAC ACCTTTTCAT  
 60 CCAGCCTTAA TTTCTGTCTC CATAACTACT CTATCCCACG ATGCAGTATT GTATCATTA TATTAGTGT GCTTGTGACC  
 TCCTTATGTA TTCTCAATTA CCTGTATTG TGCAATAAAT TGGAAATAAG TAACTIGATT TCTTATCTGT GTTTGTGTTG  
 GCATGCAAGA TTAGGTACT TATCAAGATA ATGGGGAATT AAGGCATCAA TAAATGATG CCAAAGACCA AGAGCAGTTT  
 CTGAAGTCTC CCTTTTCATC AGCTCTTTAT CAAACAGAAC ACTCTATAAA CAACCCATAG CCAGAAAAACA GGATGTAGGA  
 ACAATCACCA GCACACTCTA TAAACAACCC ATAGCCAGAA AACAGAATGT AAGGACAATC ACCAGCCATC TTTTGTCAAT  
 65 AATTGATGGA ATAGAGTTGA AAGGAACTGG AGCATGAGTC ATATTGACC AGTCAGTCTC CACTCTTATT TACTTGCTAT  
 GTAAACTTGA GAAAGCTTTT TTCTCTTTGT GAACCTCAGG TTTTACATCT GAAAAAGAGA AATTTGGAAC AAAAGATTCC  
 TAACTGGTCT TCTGTCTCT ATATCTGTG ATTTTCAAT ATTTAGGATT TTTGGTAAAT ACAATTACTT AGTTTGTGGT  
 TGAGATAGCA ACACGAATCA GAACTATTG GTGGACATAT TTTCAAAGGA GTAGCTCTCC ACTTTGGGTA AAGAAGTGAT  
 GCNGGTCTGT GTGGCTCAGC CCTGTAATCC CAGCACTTTA GGGAGGCCAA GGCGGGTGG TACAGAGGTC AGGAGATCGA  
 70 GACCATCCTG GCTAACACGG TGAACCCCG TCTCTACTAA AAAATACAAA AAATTAGCCA GCGGTGGTGG GCGGCGCTG  
 TAGTCCACG TACTCGGGAG GCTGAGGCAG GAGAATGGCA TGAACAGGG AGGCGGAGCT TGCCGTGAGC CGAGATAGCG  
 CCCTGCGAGT CCCTCTGGG CAAAAGAGCA AGACTCGCT TCAAAAAAAA AAAAAAAGAA AAAAAAAGAA GTGTGTGAGG  
 TAGCAGGACA CCTGCAACAA TAATATTTT CTAAATCCCT CTGAAAAATG CTAATCAAAG GGTTTTTTTC CTAAAAATG  
 TCTTAGAAAT AAAATTTCCC CTTTGGGAGA CCGAGGCTGG CAGATCACGA GTTCAGGAGA TAGAGACCAC GGTGAAACCC

- CGTCTCTACT AAAAATACTA AAAATTAGCC GGGGNGTGGT GGTGGGTACA CCTGTAGTCC CAGCTACTTG GAGGCTGAGG  
CTGGAGAATC ACGTGAAC-3' (FRAG. NO: ) (SEQ ID NO:11873)
- Human Histidine Decarboxylase Nucleic Acid and Antisense Oligonucleotide Fragments**
- 5'-TCT CCC TTG GGC TCT GGC TCC TTC TC TCT CTC TCC CTC TCT CTC TGT CGC CTC CGC CCT GGC TGC TGG GGT GGT  
GGT GC TTT TGT TGT TCC TTG CTG CC GCC CCG CTG CTT GTC T TC CTC G CTC TGT CCC TCT CTC TCT GTB CTC CTC BGG  
CTC CBT CBT CTC CCT TGG GC-3' (FRAG. NO:1700) (SEQ ID NO:11082)
- 5'-GGC TCT GGC (FRAG. NO:1701) (SEQ ID NO:11083)
- 5'-CCC TTG G (FRAG. NO:1702) (SEQ ID NO:11084)
- 5'-TT TGT TCT TCC (FRAG. NO:1703) (SEQ ID NO:11085)
- 10 5'-TCT CCC TTG GGC TCT GGC TCC TTC TC-3' (FRAG. NO:1024) (SEQ ID NO:10403)
- 5'-TCT CTC CTC TCT TCT CTC TGT -3' (FRAG. NO:1025) (SEQ ID NO:10404)
- 5'-CGC CTC CGC CCT GGC TGC TGG GGT GGT GGT GC-3' (FRAG. NO:1026) (SEQ ID NO:10405)
- 5'-TTT TGT TCT TCC TTG CTG CC-3' (FRAG. NO:1027) (SEQ ID NO:10406)
- 5'-GCC CCG CTG CTT GTC T TC CTC G-3' (FRAG. NO:1028) (SEQ ID NO:10407)
- 15 5'-CTC TGT CCC TCT CTC TGT CTC CTC BGG CTC CBT CBT CTC CCT TGG GC (FRAG. NO:1029) (SEQ ID NO:10408)
- Human Beta Tryptase Nucleic Acid and Antisense Oligonucleotide Fragments**
- 5'-CTT GCT CCT GGG GGC CTC CTG GTC CCT CCG GGT GTT CCC GGC GGG CCT GGC CTG GGG CBG GGG CCG CGT BGG CGC  
GGC TCG CCB GGB GGB GGC GCB GCB GCB GCB GBT TCB TCG-3' (FRAG. NO:1704) (SEQ ID NO:11086)
- 5'-GCT CCT GGG GGC CT-3' (FRAG. NO:1705) (SEQ ID NO:11087)
- 20 5'-CGT BGG CGC-3' (FRAG. NO:1706) (SEQ ID NO:11088)
- 5'-T GGC CTG GGG-3' (FRAG. NO:1707) (SEQ ID NO:11089)
- 5'-CTT GCT CCT GGG GGC CTC CTG-3' (FRAG. NO:1030) (SEQ ID NO:10409)
- 5'-GTC CCT CCG GGT GTT CCC GGC-3' (FRAG. NO:1031) (SEQ ID NO:10410)
- 5'-GGG CCT GGC CTG GGG CBG GGG CCG CGT BGG CGC GGC TCG CCB GGB CGG GCB GCG CCB GCB GCB GBT TCB GCB  
TCC TGG-3' (FRAG. NO:1032) (SEQ ID NO:10411)
- 25 **Human Tryptase-I Nucleic Acid and Antisense Oligonucleotide Fragments**
- 5'-CTT GCT CCT GGG GGC CTC CTG GTC CCT CTG GCT G TT CCC GGC CCT GGB CTG GGG CBG GGG CCG CGT BGG CGC GGC  
TCG CCB GGB CGG GCB GCG CCB GCB GCB GCB GGC TCB GCB TCC TGG CCB CGG BBT TCC-3' (FRAG. NO: 1708) (SEQ ID  
NO:11090)
- 30 5'-CT CCT GGG GGC CTC CTG-3' (FRAG. NO:1709) (SEQ ID NO:11091)
- 5'-B TCC TGG CCB CGG BBT TCC -3' (FRAG. NO:1710) (SEQ ID NO:11092)
- 5'-GTC CCT C-3' (FRAG. NO:1711) (SEQ ID NO:11093)
- 5'-CTT GCT CCT GGG GGC CTC CTG-3' (FRAG. NO:1033) (SEQ ID NO:10412)
- 5'-GTC CCT CTG GCT G TT CCC GGC-3' (FRAG. NO:1034) (SEQ ID NO:10413)
- 35 5'-CCT GGB CTG GGG CBG GGG CCG CGT BGG CGC GGC TCG CCB GGB CGG GCB GCG CCB GCB GCB GGC TCB GCB TCC  
TGG CCB CGG BBT TCC -3' (FRAG. NO:1035) (SEQ ID NO:10414)
- Human Prostaglandin D Synthase Nucleic Acid and Antisense Oligonucleotide Fragments**
- 5'-GGT GTG CGG GGC CTG GTG CC CCT GGG CCT CGG GTG CTG CCT GT GCG CTG CCT TCT CCT GGT GTC CTC GCC GGG  
GCC CTT GCT GCC CTG GCT GT GCC CTG GGG GTC TGG GTT CGG CTG T CCC CBG CBG GBC CBG TCC CBT CCB CBG CGT  
GTG BTG BGT BGC CBT TCT CCT GCB GCC GGG-3' (FRAG. NO:1712) (SEQ ID NO:11094)
- 40 5'-T TCT CCT GCB GCC GGG -3' (FRAG. NO:1713) (SEQ ID NO:11095)
- 5'-CTT GCT GCC CTG GCT GT-3' (FRAG. NO:1714) (SEQ ID NO:11096)
- 5'-TCT TCT CCT GG-3' (FRAG. NO:1715) (SEQ ID NO:11097)
- 5'-GGT GTG CGG GGC CTG GTG CC-3' (FRAG. NO:1036) (SEQ ID NO:10415)
- 45 5'-CCT GGG CCT CGG GTG CTG CCT GT-3' (FRAG. NO:1037) (SEQ ID NO:10416)
- 5'-GCG CTG CCT TCT TCT CCT GG-3' (FRAG. NO:1038) (SEQ ID NO:10417)
- 5'-GTC CTC GCC GGG GGC CTT GCT GCC CTG GCT GT-3' (FRAG. NO:1039) (SEQ ID NO:10418)
- 5'-GCC CTG GGG GTC TGG GTT CGG CTG T-3' (FRAG. NO:1040) (SEQ ID NO:10419)
- 5'-CCC CBG CBG GBC CBG TCC CBT CCB CBG CGT GTG BTG BGT BGC CBT TCT CCT GCB GCC GGG -3'  
(FRAG. NO:1041) (SEQ ID NO:10420)
- 50 **Human Cyclooxygenase-2 Nucleic Acid and Antisense Oligonucleotide Fragments**
- 5'-GGG CGC GGG GCB GCB TCG C TTT GGG CTT TTC TCC TTT GGT T TGB GCG CCB GGB CCG CGC BCB GCB GCB GGG CGC  
GGG GCB GCB TCG CBG CGG CGG GCB GGG-3' (FRAG. NO: 1716) (SEQ ID NO:11098)
- 5'-G GCB GGG -3' (FRAG. NO: 1717) (SEQ ID NO:11099)
- 55 5'-TCC TTT GGT T-3' (FRAG. NO:1718) (SEQ ID NO:11100)
- 5'-GGG CGC GGG GCB GCB TCG C-3' (FRAG. NO:1042) (SEQ ID NO:10421)
- 5'-TTT GGG CTT TTC TCC TTT GGT T-3' (FRAG. NO:1043) (SEQ ID NO:10422)
- 5'-TGB GCG CCB GGB CCG CGC BCB GCB GCB GGG CGC GGG GCB GCB TCG CBG CGG CGG GCB GGG -3'  
(FRAG. NO:1044) (SEQ ID NO:10423)
- 60 **Human Eosinophil Cationic Protein Nucleic Acid and Antisense Oligonucleotide Fragments**
- 5'-CCT CCT TCC TGG TCT GTC TGC CBG BCB BBT TTG GGB BGT GBB CBG TTT TGG BBC CBT GTT TCC CBG TCT CTG BGC  
TGT GGC-3' (FRAG. NO: 1719) (SEQ ID NO:11101)
- 5'-TTC TCC TTT GGT T-3' (FRAG. NO:1720) (SEQ ID NO:11102)
- 5'-T TTC TCC TTT GGT T-3' (FRAG. NO:1721) (SEQ ID NO:11103)
- 65 5'-GGG CGC GGG GCB GCB TCG C-3' (FRAG. NO:1042) (SEQ ID NO:10421)
- 5'-TTT GGG CTT TTC TCC TTT GGT T-3' (FRAG. NO:1043) (SEQ ID NO:10422)
- 5'-TGB GCG CCB GGB CCG CGC BCB GCB GCB GGG CGC GGG GCB GCB TCG CBG CGG CGG GCB GGG -3'  
(FRAG. NO:1044) (SEQ ID NO:10423)
- Human Eosinophil Derived Neurotoxin Nucleic Acid and Antisense Oligonucleotide Fragments**
- 70 5'-GCC CTG CTG CTC TTT CTG CT TCC CTT GGT GGG TTG GGC C GCT GGT TGT TCT GGT GTT C TTG CTG CCC CTT CTG TCC C  
TGT TTG CTG GTG TCT GCG C 5'-CCC CBB CBG BBG BBG CBG BCB BBT TTG GGB BGT GBB CBG TTT TGG BBC CBT GTT TCC  
TGT-3' (FRAG. NO: 1722) (SEQ ID NO:11104)
- 5'-TTC CTG T-3' (FRAG. NO:1723) (SEQ ID NO:11105)

5'-CTC TTT CTG CT-3' (FRAG. NO: 1724) (SEQ ID NO:11106)  
 5'-CCC CTT CTG TCC C-3' (FRAG. NO:1725) (SEQ ID NO:11107)  
 5'-GCC CTG CTG CTC TTT CTG CT-3' (FRAG. NO:1047) (SEQ ID NO:10424)  
 5'-TCC CTT GGT GGG TTG GGC C-3' (FRAG. NO:1048) (SEQ ID NO:10425)  
 5'-GCT GGT TGT TCT GGG GTT C-3' (FRAG. NO:1049) (SEQ ID NO:10427)  
 5'-TTG CTG CCC CTT CTG TCC C-3' (FRAG. NO:1050) (SEQ ID NO:10426)  
 5'-TGT TTG CTG GTG TCT GCG C-3' (FRAG. NO:1051) (SEQ ID NO:10428)  
 5'-CCC CBB CBG BBG BBG CBG BCB BBT TTG GGB BGT GBB CBG TTT TGG BBC CBT GTT TCC TGT-3' (FRAG. NO:1052) (SEQ ID NO:10429)

# 10 **Human Eosinophil Peroxidase Nucleic Acid and Antisense Oligonucleotide Fragments**

5'-GCG CTC GGC CTG GTC CCG G GGG TCT CCT CTT GTT GC TTG CGC CTC CTG CTG GGG GT CC CTC TGT TCT TGT TTT  
 GGG GGC GGG CCC GGC CGT TGT CTT G GTT TGG GGG TTT CCG TTG GGG TTC TCC TGG CCC GGG CCT TGC CC GGC CGT  
 GGT CCC GGC TTC GTTCTT GTC TCC GTC TCG GCT CTT CTG GGG CCT TGC GCT GTC TTT GGT G 5'-GCB CCG TCC BGT GBT  
 GGT GCG GTB CTT GTC GCT GCB GCG CTC GGC CTG GTC CCG GBG BGC CACCGCTCCT GTCAGCCAAC AAATATCCAT  
 15 TGAGCGACAC CTGTGTCCCA GGTGCTGCTC TGGGCCCTGG GAGAAGTGCA TCAGTGGGCT TGGTAGTAGA GGGTAGGGAT  
 GGAGTGAAGG GTAGGCAGGA AGAATGTCCC CAGGCTGGTA GGAGGTGGGG TGGGGGGTTT CAGTCTCAAA ACTCCCATGA  
 AAACAGAGA GAAATTTCAG AACTCCACCC AAGAGGCTGG GTTCTAGGG CCCAGAGCTG CCTTCCCCCA CCTAGAAATG  
 GGCTATAAAA GTCCCTTCCC AGCTACGTCC AGAGAAGAGC TGGAGGAAGT GAGAGGTGGG CTGGGGGTCC TCAAGGCAAGG  
 AGGGGAGCAG AGGATCTCC CGTGCAGGCT GTGGATGTCA CTCACTTCCC AGCTGGTGAA GCCTCGCTGC AGAGATGCAT  
 20 CTGCTCCAG CCTGGCAGG GGTCTGGCC ACACCTGCTC TCGCCAGCC CTGTGAGGGC ACTGACCCAG GTAATAGTCC  
 CTAGACAGG CAAGGAGGAG GGAGGGGAAA TGGAAAGGGA AGCACTTGGG TCTTGGAGGG GGCTTTGTGG CTGTGGAAC  
 CCTGAGTCCC CATCTCTTIG AACAGCTCC CCTGGGGCAG TGGAGACCTC GGTCCTGCGA GACTGCATAG CAGAGGCCAA  
 GTTGCTGGTG GATGCTGCCT ACAATTGGAC CCAGAAGAGG TGGACTTGGG TCTGGGGGCT GCATGGGCT GGGAGGATCA GT  
 TAATACTTGT TGGGCTCAGG GAGCCCATGT CCGGTCTGA TGTATTTC CCACCAAGTC CGGGCTGCT CCAACCCAGAT  
 25 TGTGCGCTTC CCAATGAGA GACTGACCTC CGACCGTGGC CGAGCCCTCA TGTTCATGCA GTGGGGCCAG TTCATTGACC  
 ATGACCTGGA CTCTTCCCCG GAGTCCCCGG CCAGAGTGGC CTTCACCTGCA GGCCTTGACT GTGAGAGGAG CTGGCCCCAG  
 CTGCCCTCT GCTTCTCCAT -CAAGGTACCT ACCCTCAGCC AATCTCCCAT GCGCTTGTGT GGCTTCCCC AAAGGCAAGG  
 TGCTGGGGGT GGGGATCTGG AAGACTGGAG CACCATCCTT AAGGAGCTGC CTGTGGAGCT AGGGATATGAG ACAGAGACAC  
 AAG CACTGTCTCC TCTTCCATCT CAGATCCAC CCAATGACCC CCGCATCAAG AACCAGCGTG ACTGCATCCC TTCTTCCCG  
 30 TCGGCACCT CATGCCCCA AAACAAGAAC AGAGTCCGA ACCAGATCAA CGCGCTCACC TCCTTTGTGG ACGCCAGCAT  
 GGTGTATGGC AGTGAGGTCT CCTCTCGCT GCGGTCCGC AACCGGACCA ACTACCTGGG GCTGCTGGCC ATCAACCAGC  
 GCTTTCAAGA CAACGGCCCG GCCCTGCTGC CCTTCGACAA CTGACAGAT GACCCCTGTC TCCTACCAA CCGCTCGGCG  
 CGCATCCCT GCTTCTGGC AGGTACAGCA GGGAGGAAGG TGTGTCTTC CCAGGAACA GCCATCCCTG GGGTCCCAAC  
 TGGGAAGCAA TGGTGGGATG TGGTGAAGGT ACATGGTTTG GGACCTCAGT ATTAGGCACA CCATAAGCAT GGATCTGTGC AC  
 35 TGAAGAGATG GAGGTCCAGT GAGGGCCAGG AGTTTGGGCC ACCCGTCTC TCCTATCCCC AGCCCTGGGT CTACCTTGGT  
 AGAAAGACAT TTCTCTGGGA AAGGTGCAG TAAATCTGAG CTGTGGGTTT TCAAGGTGAC ACCCGATCAA AAGAAACCCC  
 CAAACTGGCA CCAATGCACA CCTCTTTAT GCGAGAGCAG AACCGGCTGG CCACCGAGCT GAGACGCTG AATCCCCGGT  
 GGAATGAGA CAAACTGTAC AATGAGGCTC GGAAGATCAT GGGGGCCATG GTCCAGGTAA GGAGCTCTGC ATCCAGCAT  
 CCCCC CTITGTATCT CCACCCACCA ATAGTAAAT AATGTTGTCA CATTGACGT GATGACATA AAGAATATGT  
 40 CTGAGCCACC CTTTGAAGA GCAAGGGTAT GGGTGAGTAG CCTTGGGGA ATGTCTCTCC TGTCTTCCCT TCCAGATCAT  
 CACTACCGA GACTTCTTGC CCTGTGTCT GGGCAAGGCC CGGGCCAGGA GAACCCCTGG GCACCTACAGG GGGTACTGCT  
 CCAATGTGGA CCCACGGGTG GCCAATGTCT TCACCTGGC CTTCCTCTTT GGCCACACAA TGCTCCAGCC CTTCATGTTT  
 CGCTTGGACA GCTAGTACCG GGCCTCCGCA CCAACTCGC ATGTCCCACT TAGCTCTGCC TCTTTGCCA GCTGGCGGAT  
 CGTGTATGAA GGTGACCAAG TTTTCCAGGG GGCAATGGG GGTGAGGGTG GGGAGCATGC CCTCCCTAG GTGG  
 45 TCCAGCTGCT TCATGTCTCT CCAGAATCT GTTCTCTGAC AAACGTTACT AACATACCCG ACTGGCTTGT CCAGCTCTGG  
 GCTAGCTTGG CATCATGTGA TAACCCAAGT AGCTTCCAG AGGCTGGTCC AATCTGTGCT GCTCACATCT CTGCCACCA  
 GGGGGCATCG ACCCATCCT CCGGGGCTC ATGGCCACCC CTGCCAAGCT GAACCGTCAG GATGCCATGT TAGTGGATGA  
 GCTCCGGGAC CGGCTGTTTC GGCAAGTGAG GAGGATTTGG CTGGACCTGG CAGCTCTCAA CATGCAACGA AGCCGGGACC  
 ACGGCTTCC AAGTGAGGGG GCTGTCCACC TCTTCTCCA GCTTTGCTCG GGCCAGGCTG CTCGAAGGGT TCTGGGAAGA  
 50 CCCTGGTACC CCACTGCTG GTAGGTTCTG GTGGCAGAAA CGAGGTGTTT TCACCAAAAAG ACAGCGCAAG GCCTGAGCA  
 GAAATTTCTT GTCTCGAATT ATATGTGACA ATACCGGTAT CACCACGGTT TCAAGGGACA TCTTCAGAGC CAACATCTAC  
 CTCGGGGGTT TGTGGAATG CAGCCGTATC CCCAGGTTGA ACCTATCAGC CTGGCGAGGG ACATGAGGCT TCTGACGTA  
 AGGGGAGGCC ACCTCCAGCA CCTTGGGCTG GTTAAGCCTC ACATCTTCC CTGGATGGAT GGCTGAGTCC TCTAGGTCT  
 CTAAGCAGAG AAAACAGAAC TTGTCACTAG GTACTCTTC CAAGTGGCTT CCAATGTGC TAGTTTCTGG GCTGACAGTC  
 55 AATTCCAGGC CTAAGGACTT TGGGGGGA AAA TTAGGAGCAT CCAACTA GAATTCCGTG GCCAGGACCC CTGCCAGGGC  
 ACTGACCCAG CCTCCCTGG GGCAGTGGAG ACCTCGGTCC TCGAGACTG CATAGCAGAG GCCAAGTGC TGGTGGATGC  
 TGCTACAAAT TGGACCCAGA AGAGCATCAA GCAGCGGCT CGCAGCGGTT CAGCCAGCCC CATGGACCTC CTGTCTACT  
 TCAACAACCC GGTAGCAGCC ACCAGGACAG TTGTTCGGGC CGCAGATTAT ATGCATGTGG CTTTGGGGCT GCTTGAAGAG  
 AAGTTACAAC CCCAGCGGTC CGGACCTTC ATTGTCACTG ATGTGCTAAC AGAACCACAG CTGCGGCTGC TGTCCAGGC  
 60 CAGTGGCTGT GCTCTCCGG ACCAGGCCGA GCGCTGCAGC GACAAAGTACC GCACCATCAC TGGACGGTGC AACAACAAGA  
 GGAGACCTT GCTAGGGGCC TCCAACCAGG CTCTGGCTCG CTGGCTGCCC GCGGAGTATG AGGATGGGT GTCGCTCCCC  
 TTGGGCTGGA CCCCCAGCAG GAGGCGCAAT GGCTTCTTC TCCCTCTTGT CCGGGCTGTC TCCAACCAGA TTGTGCGCTT  
 CCCCCAATGAG AGACTGACCT CCGACCGTGG CCGAGCCCTC ATGTTTCATGC AGTGGGGCCA GTTCAATTGAC CATGACCTGG  
 ACTTCTCCCC GGAGTCCCCG GCCAGAGTGG CCTTCACTGC AGGCGTTGAC TGTGAGAGGA CTGCGGCCCA GCTGCCCCCC  
 65 TGCTTTCCCA TCAAGATCCC ACCCAATGAC CCCCCATCA AGAACCAGCG TGAATGCATC CTTTCTTCC GCTCGGCACC  
 CTCATGCCCC CAAAACAAGA ACAGAGTCCG CAACAGATC AACGCGCTCA CCTCTTGT GTGACGCCAG ATGGTGTATG  
 GCAGTGAAGT CTCCCTCTCG CTGCGGCTCC GCAACCGGAC CAATACCTG GGGCTGCTGG CCATCAACCA GCGCTTTCAA  
 GACAAACGCC GGGCCCTGCT GCCCTTCGAC AACCTGCAGC ATGACCCCTG TCTCTTACC AACCGCTCG GCGCATCTCC  
 CTGCTTCTCG GCAGGTGACA CCGATCAAC GGAACCCGCC AAATGGCAG CCATGCACAC CCTCTTATG CGAGAGCACA  
 70 ACCGGCTGGC CACCGAGCTG AGACGCTGA ATCCCGGTG GAATGGAGAC AAACGTGACA ATGAGGCTCG GAAGATCATG  
 GGGGCAATGG TCCAGATCAT CACCTACCGA GACTTCTGC CCTGGTTCT GGGCAAGGCC CCGGCCAGGA GAACCTTGGG  
 GCACTACAGG GGGTACTGCT CCAATGTGGA CCCACGGGTG GCCAATGTCT TCACCTGGC CTTCGCTTT GGCACACAA  
 TGCTCCAGCC CTTCATGTTT CGCTTGGACA GTCACTCCG GGCCTCCGCA CCAACTCGC ATGTCCACT TAGCTCTGCC  
 75 TTCTTGGCA GCTGGCGAT CGTGTATGAA GTCGACATCG ACCCATCTT CCGGGGCTC ATGGCCACCC CTGCCAAGCT  
 GAACCGTCAG GATGCCATGT TAGTGGATGA GCTCCGGGAC CGGCTGTTTC GGCAAGTGA GAGGATTGGG CTGGACCTGG

CAGCTCTCAA CATGCAACGA AGCCGGGACC ACGGCCTTCC AGGGTACAAT GCTTGGAGGC GCTTCTGTGG GCTCTCCAG  
CCCCGGAAATT TGGCACAGCT TAGCCGGGTG CTGAAAAACC AGGACTTGGC AAGGAAGTTC CTGAATTTGT ATGGAACACC  
TGACAACATT GACATCTGGA TTGGGGCCAT CGCTGAGCCT CTTTGTGCCG GGGCTCGAGT GGGGCCCTCT CTGGCTTGTG  
5 AAGGCGCTGA GCAGAATTTT CTTGTCTCGA ATTATATGTG ACAATACCGG TATCACCACG GTTTCAAGGG ACATCTTCAG  
AGCCAACATC TACCCTCGGG GCTTTGTGAA CTGCAGCCGT ATCCCCAGGT TGAACCTATC AGCCTGGCGA GGGACATGAG  
GCTTCTGCGA GAGTCTATCC CAAGTCTCCA ACTTTTGGAG ACAAGGGGAA GGGGAGGACC ATGAGGCTGC CTTGTCTCCC  
TGGAGCAAGT GCAGGCTCGT GACGCTTCTG CTGGCTACAG CTCAGAGCTG GGTTCGCCAG CCAGGAGTGA AGGCTGGGGG  
CTCCTATCAG CAATGGACCT TCCGCTTGG GAGCCTCTTA GGTATTAGGC TATGAATCAG CGCCACGTGC AAAGGCTTGG  
10 GAGCCAAGCC ATGTGGTCTT GCACCCCAAG CAAGAAAAGT CAGCTGGAGG GTTTACAGCA CTTTCTACTG TTTCCCAGCC  
CTCCCTCCCC TCCCTACCA TGAATAAGAG ACCACTCGGT CCTAGCCTCC AGACACCCCA CAATACTCCT CTGAGACTGA  
GGCCAGGCAG CATGCTCTGC TTCTACCAAT AAAGCACTGC CGGAATTC-3' (FRAG. NO: 1726) (SEQ ID NO:12377)  
5'-CACCGCTCCT GTACGCCAAC AAATATCCAT TGAGCGACAC CTGTGTCCCA GGTGCTGCTC TGGGCCCTGG GAGAAGTGCA  
TCAGTGGGCT TGGTAGTGA GGGTAGGGAT GGAGTGAAGG GTAGGCAGGA AGAATGTCCC CAGGCTGGTA GGAGGTGGGG  
15 TGGGGGGTTT CAGTCTCAA ACTCCCATGA AAACCAGAGA GAAGTTTCAG AACTCCACCC AAGAGGCTGG GTTTCTAGGG  
CCCAGAGCTG CCTGCCCA CCTAGAAATG GGCTATAAAG GTCCCTTCCC AGCTACGTCC AGAGAAGAGC TGGAGGAAGT  
GAGAAGTCTG CTGGGGTCTC TCAAAGTGAG AGGGGACAG AGGATCCTCC CGTGCAGGCT GTGGATGTCA CTCATCTCCC  
AGCTGGTGAA GCCTCGCTGC AGAGATGCAT CTGCTCCAG CCTGGCAGG GGTCTGGCC AACTCGTCC TCGCCAGCC  
CTGTGAGGGC ACTGACCCAG GTAATAGTCC CTTAGACAGG CAAGGAGGAG GGAGGGGAAA TGGAAAGGGA AGCACTTGGG  
20 TCTTGGAGGG GGTCTGTGG CTTGCTGAAC CTTGCTTCCC CATCTCTTTG AACAGCCTCC CTTGGGGCAG CCTGGGACCTC  
GGTCTGCGA GACTGCATAG CAGAGGCCAA GTTGCTGGT GATGCTGCCT ACAATTGGAC CCAGAAGAGG TGGACTTGGG  
TCTGGGGGCT GCATGGGCTG GGGAGGATCA GT-3' (FRAG. NO: ) (SEQ ID NO:11852)  
5'-TAATACCTTG TGGGTCAGG GAGCCCATGT CCGGTGCTGA TGTATTTC CCACCAGGTC CGGGCTGTCT CCAACCAGAT  
TGTGCGCTTC CCAATGAGA GACTGACCTC CGACCGTGGC CGAGCCCTCA GTTTCATGCA GTGGGGCCAG TTCATTGACC  
25 ATGACCTGGA CTTCTCCCG GAGTCCCGG CAGGCTGTGG CTTCACTGCA GCGGTGACT GTGAGGAGC CTGCGCCAGC  
TGCCCCCTT GCTTCCCAT CAAGGTACCT ACCCTCAGC AATCTCCAT GCCCTTGTGT GGCCTCCCG AAAGGCAAGG  
TGCTGGGGT GGGGATCTGG AAGACTGTAG CACCATCTT AAGGAGCTGC CTGTGGAGCT AGGGTATGAG ACAGAGACAC  
AAG-3' (FRAG. NO: ) (SEQ ID NO:11853)  
5'-CACTGTCTCC TCTTCCATCT CAGATCCAC CCAATGACCC CCGCATCAAG AACCAGCGTG ACTGCATCCC TTTCTTCCGC  
30 TCGGACCCCT CATGCCCA AAACAAGAAC AGAGTCCGCA ACCAGATCAA CGCGCTACC TCCTTTGTGG ACGCCAGCAT  
GGTGTATGGC AGTGAGGTCT CCTCTCGCT GCGGCTCCG AACCAGGACA ACTACCTGGG GCTGTGGCC ATCAACCAGC  
GCTTTCAAGA CAACGGCCCG GCCCTGTGC CTTTCGACAA CTTGCACGAT GACCCCTGTC TCCTACCAA CCGCTCGGCG  
CGCATCCCT CTTCTCTGC AGGTACAGCA GGGAGGAAGG TGGTGTCTTC CCAGGAAACA GCCATCCCT GGGTCCCAAC  
TGGGAAGCAA TGGTGGGATG TGGTGAAGT ACATGTTTG GACCTCAGT ATTAGGCACA CCATAAGCAT GGATCTGTGC AC-3'  
35 (FRAG. NO: ) (SEQ ID NO:11854)  
5'-TGAAGAGATG GAGGTCCAGT GAGGGCCAGG AGTTTGGCCC ACCCGTCTC TCCATCCCC AGCCCTGGGT CTACCTGGT  
AGAAAGACAT TTCTCTGGGA AAGGTGCGAG TAAATCTGAG CTTGGGGTTT TCAAGGTGAC ACCCGATCAA CGGAACCCCT  
CAAATGGCA GCCATGCACA CCTCTTTAT GCGAGAGCAT AACCAGGCTGG CCACCGAGCT GAGACGCTG AATCCCCGGT  
GGAATGGAGA CAAACTGTAC AATGAGGCTC GGAAGATCAT GGGGGCCATG GTCCAGGTAA GGAGCTCTGC ATCCAGCAT  
40 CCCCC-3' (FRAG. NO: ) (SEQ ID NO:11855)  
5'-CTTTGTATCT CCAACCCACA ATAGTAAATT AATGTTGTCA CATTTGACGT GATGACAATA AAGAATATGT CTGAGCCACC  
CTTTGAAAG CAAGGGGTAT GGGTGAAGT GCTCTGGGGA ATGTTCCCTC TGCTTCCCT TCCAGATCAT CACCTACCGA  
GACTTTCTGC CCTGGTTCT GGGCAAGGCC CGGGCCAGGA GAACCTGGG GCACTACAGG GGGTACTGCT CCAATGTGGA  
CCCAGGGGTG GCCAATGTCT TCACCTGTGC CTTCCGCTTT GGGCACACAA TGCTCCAGCC CTTCATGTT CCGTGGGACA  
45 CTGAGTGGT GGCCTCCGCA CCAACTCGC ATGTCCCAT TAGCTCTGCC TTCTTTGCCA GCTGGCGGAT CCGTATGATA  
GGTGACCAGG TTTTCCAGG GGCAAATGGG GGTGAGGGTG GGGAGCATGC CCTCCCTAG GTGG-3' (FRAG. NO: ) (SEQ ID  
NO:11856)  
5'-TCCAGCTGCT TCATGTCTCT CCAGAACTCT GTTCTCTGAC AAACGTTACT AACATACCCG ACTGGCTGTG CCAGCTCTGG  
GCTAGCTTGG CATCATGTGA TAACCCAAGT AGCTTCCAG AGGCTGGTCC AATCTGTGCT GCTCACATTC CTTGCCACCA  
50 GGGGGCATCG ACCCATCCT CCGGGGCCCTC ATGGCCATCC CTGCCAAGCT GAACCGTCAG GATGCCATGT TAGTGGATGA  
GCTCCGGGAC CGGCTGTTT GGCAAGTGAG GAGGATAGG CTGACCTGG CAGCTCTAA CAGTCAACGA AGCCGGGACC  
ACGCCCTTCC AGGTGAGGGG GCTGTCCAG TCTTCTCCCA GCTTTGCTCG GGCCAGGCTG CTCAAGGGGT TCTGGGAAGA  
CCTGTGTACC-3' (FRAG. NO: ) (SEQ ID NO:11857)  
5'-CGACTGCTG GTAGTTCTG GTGGCAGAAA CGAGGTGTTT TCACCAAAAG ACAGCGCAAG GCCTGAGCA GAATTTCTTT  
55 GTCTCGAATT ATATGTGACA ATACCGGTAT CACCACGGTT TCAAGGGACA TCTTCAGAGC CAACATCTAC CTTGGGGGCT  
TTGTGAACTG CAGCCGTATC CCAAGGTGTA ACCTATCAGC CTGGCGAGGG ACATGAGGCT TCTGCAGGTA AGGGGAGGCT  
ACCTCCAGCA CCCTGGGCTG GTTAAGCCTC ACATCTTCT CTGGATGGAT GGCTGAGTCC TCTTAGGTCT CTAAGCAGAG  
AAAACAGAAC TTGTCACTAG GTACTCTTC CAAGTGGCTT CCAATGTGC TAGTTTCTGG GCTGACAGTC AATTCCAGGC  
CCTAGGACTT TGGGGGGA TTAGGAGCAT CCAACTA-3' (FRAG. NO: ) (SEQ ID NO:11858)  
60 5'-GAATTCGGTG GCCAGGACCC CTGCCAGGGC ACTGACCCAG CCTCCCTGG GGCAGTGGAG ACCTCGGTCC TGGGAGACTG  
CATAGCAGAG GCCAAGTTGC TGGTGGATGC TGCCTACAAT TGGACCCAGA AGAGCATCAA GCAGCGGCTT CGCAGCGGTT  
CAGCCAGCCC CATGGACCTC CTGTCTACT TCAAACAACC GGTAGCAGCC ACCAGGACAG TTGTTCCGGC CGCAGATTAT  
ATGCATGTGG CTTTGGGGCT GCTTGAAGAG AAGTTACAAC CCCAGCGGTG CGGACCTTC ATTGTCACTG ATGTGCTAAC  
65 AGAACACAG CTGCGGCTGC TGTCCAGGC CAGTGGCTGT GCTCTCCGG ACCAGGCCGA GCGCTGCAGC GACAAGTACC  
GCACCATCAC TGGACGGTGC AACAACAAGA GGAGACCTT GCTAGGGGCC TCCAACCAAG CTCTGGCTCG CTGGCTGCC  
CCCGAGTATG AGGATGGGCT GTGCTCCCC TTCGGCTGGA CCCCCAGCAG GAGGCGCAAT GGCTTCTTC TCCCTTTGT  
CCGGGCTGTC TCCAACAGA TTGTGCGCTT CCCCAGTGA AGACTGACCT CCGACCGTGG CCGAGCCCTC ATGTTCACTG  
AGTGGGGCCA GTTCAATTGAC CATGACCTGG ACTTCTCCC GGAGTCCCCG GCCAGAGTGG CCTTCACTGC AGGCGTTGAC  
70 TGTGAGAGGA CTTGCGCCCA GCTGCCCCC TGCTTTCCCA TCAAGATCCC ACCCAATGAC CCCCAGTCA AGAACGCTCA  
TGACTGCATC CTTTCTTCC GCTCGGCACC CTCACTGCC CAAAACAAGA ACAGAGTCCG CAACCAAGATC AACCGCTCA  
CCTCTTTGT GGACGCCAGC ATGGTGTATG GCAGTGAAGT CTCCCTCTCG CTGCGGCTCC GCAACCGGAC CAACTACCTG  
GGGCTGTGG CCATCAACCA GCGCTTTCAA GACAACGGCC GGGCCCTGCT GCCCTTCGAC AACCTGCAGC ATGACCCCTG  
TCTCTCAC CAACTGCTCG CGGCATCCC CTGCTTCTG GCAGGTGACA CCGATCAAC CCGAAACCCG AAAGTGGCAG  
CCATGCACAC CCTCTTATG CGAGAGCACA ACCGGCTGGC CACCGAGCTG AGACGCTGA ATCCCGGTG GAATGGAGAC  
75 AAAGTGTACA ATGAGGCTCG GAAGATCATG GGGGCCATGG TCCAGATCAT CACCTACCGA GACTTCTGCT CCTGTGTTCT



- GGGCAAGGCC CGGGCCAGGA GAACCTGGG GCACTACAGG GGGTACTGCT CCAATGTGGA CCCACGGGTG GCCAATGTCT  
 TCACCCCTGGC CTTCGGCTTT GGCCACACAA TGCTCCAGCC CTTCATGTTT CGCTTGGACA GTCAGTACCG GGCTCCGCA  
 CCAACTCGC ATGTCCCACT TAGCTCTGCC TTCTTTGCCA GCTGGCGGAT CGTGTATGAA GGGGGCATCG ACCCCATCCT  
 CCGGGGCCCTC ATGGCCACCC CTGCCAAGCT GAACCGTCAG GATGCCATGT TAGTGGATGA GCTCCGGGAC CGGCTGTTC  
 5 GGAAGTGAAG GAGGATTGGG CTGGACCTGG CAGCTCTCAA CATGCAACGA AGCCGGGACC ACGGCTTCC AGGGTACAAT  
 GCTTGGAGGC GCTTCTGTGG GCTCTCCAG CCCCAGGAAT TGCCACAGCT TAGCCGGGTG CTGAAAAACC AGGACTTGGC  
 AAGGAAGTTC CTGAATTTGT ATGGAACACC TGACAACATT GACATCTGGA TTGGGGCCAT CGCTGAGCCT CTTTGCCGG  
 GGGCTCGAGT GGGGCTCTT CTGGCTTGTG TGTTCCAGAA CCAGTTTCTGAG AGAGCCGAGA CGGAGACAGG TTCTGGTGGC  
 AGAACGAGGT GTTTTACCA AAGACAGCGC AAGGCCCTGA GCAGAAATTC CTGTCTCGA ATTATATGTG ACAATACCGG  
 10 TATCACCACG GTTTCAAGGG ACATCTTCAG AGCCAACATC TACCCTCGGG GCTTTGTGAA CTGCAGCCGT ATCCCCAGGT  
 TGAACCTATC AGCCTGGCGA GGGACATGAG GCTTCTGCA GAGTCTATCC CAAGTCTCCA ACTTTTGGAG ACAAGGGGAA  
 GGGGAGGACC ATGAGGCTGC CTTGTCTCC TGGAGCAAGT GCAGGCTCGT GACGCTTCTG CTGGCTACAG CTGAGAGCTG  
 GGTTCGCCAG CCAGGAGTGA AGGCTGGGG CTCTATCAG CAATGGACCT TCCGCTTGG GAGCCTCTTA GGTATTAGG  
 TATGAATCAG GCCACGTGC AAAGGCTTGG GAGCCAAGCC ATGTGGTCTT GCACCCAGG CAAGAAAGT CAGCTGGAGG  
 15 GTTTACAGCA CTTTCTACTG TTTCCAGCC CTCCCTCCC TCCTCACCA TGACTAAGAG ACCACTCGGT CTAAGCTCC  
 AGACACCCCA CAATACTCT CTGAGCCTGA GGCCAGGAG CATGCTCTGC TTCTACCAAT AAAGCACTGC CGGAATTC-3'  
 (FRAG.NO: ) (SEQ ID NO:11859)  
 5'-TC GGC CTG GTC CCG G-3' (FRAG. NO: 1727) (SEQ ID NO:11109)  
 5'-TGG GGG TTT CCG TTG-3' (FRAG. NO: 1728) (SEQ ID NO:11110)  
 20 5'-TG GTC CCG GBG BGC -3' (FRAG. NO: 1729) (SEQ ID NO:11111)  
 5'-GCG CTC GGC CTG GTC CCG G-3' (FRAG. NO:1053) (SEQ ID NO:10430)  
 5'-GGG TCT CCT CTT GTT GTT GC-3' (FRAG. NO:1054) (SEQ ID NO:10431)  
 5'- TTG CGC CTC CTG CTG GGG GT CC-3' (FRAG. NO:1055) (SEQ ID NO:10432)  
 5'-CTC TGT TCT TGT TTT GGG GGC-3' (FRAG. NO:1056) (SEQ ID NO:10433)  
 25 5'-GGG CCC GGC CGT TGT CTT G-3' (FRAG. NO:1057) (SEQ ID NO:10434)  
 5'-GTT TGG GGG TTT CCG TTG-3' (FRAG. NO:1058) (SEQ ID NO:10435)  
 5'-GGG TTC TCC TGG CCC GGG CCT TGC CC-3' (FRAG. NO:1059) (SEQ ID NO:10436)  
 5'-GGC CGT GGT CCC GGC TTC GTT GC-3' (FRAG. NO:1060) (SEQ ID NO:10437)  
 5'-CCT GTC TCC GTC TCG GCT CTT CTG-3' (FRAG. NO:1061) (SEQ ID NO:10438)  
 30 5'-GGG CCT TGC GCT GTC TTT GGT G-3' (FRAG. NO:1062) (SEQ ID NO:10439)  
 5'-GCB CCG TCC BGT GBT GGT GCG GTB CTT GTC GCT GCB GCG CTC GGC CTG GTC CCG GBG BGC -3' (FRAG. NO:1063) (SEQ  
 ID NO:10440)

#### Human Intercellular Adhesion Molecule-1 (ICAM-1)

##### Nucleic Acid and Antisense Oligonucleotide Fragments

- 35 5'-GCG CGG GCC GGG GGC TGC TGG G GGT TGG CCC GGG GTG CCC C GCC GCT GGG TGC CCT CGT CCT CTG CGG TC GTG  
 TCT CCT GGC TCT GGT TCC CC GCT GCG CCC GTT GTC CTC TGG GGT GGC CTT C GCT CCC GGG TCT GGT TCT GTT GTT  
 GGG TCC CTT TTT GGG CCT GTT GT GGC GTG GCT TGT GTG TTC GGT TTC TGC CCT GTC CTC CGG GGT CCC CGG BGC CTC  
 CCC GGG GCB GGB TGB CTT TTG BGG GGG BCB CBG BTG TCT GGG CBT TGC CBG GTC CTG GGB BCB GBG CCC CGB GCB  
 GGB CCB GGB GTG CCG GCB GCG CGG GCC GGG GGC TGC TGG GBG CCB TBG CGB GGC TGB G-3' (FRAG. NO: 1730) (SEQ  
 40 ID NO:11112)  
 5'-GGG GGC TGC TGG G-3' (FRAG. NO: 1731) (SEQ ID NO:11113)  
 5'-T GTC CTC CGG CGT CCC-3' (FRAG. NO:1732) (SEQ ID NO:11114)  
 5'-G CCB TBG CGB GGC TGB G-3' (FRAG. NO: 1733) (SEQ ID NO:11115)  
 5'-CTC TGG GGT GGC CTT C-3' (FRAG. NO:1734) (SEQ ID NO:11116)  
 45 5'-GCG CGG GCC GGG GGC TGC TGG G-3' (FRAG. NO:1064) (SEQ ID NO:10441)  
 5'-GGT TGG CCC GGG GTG CCC C-3' (FRAG. NO:1065) (SEQ ID NO:10442)  
 5'-GCC GGT GGG TGC CCT CGT CCT CTG CGG TC-3' (FRAG. NO:1066) (SEQ ID NO:10443)  
 5'-GTG TCT CCT GGC TCT GGT TCC CC-3' (FRAG. NO:1067) (SEQ ID NO:10444)  
 5'-GCT GCG CCC GTT GTC CTC TGG GGT GGC CTT C-3' (FRAG. NO:1068) (SEQ ID NO:10445)  
 50 5'-GCT CCC GGG TCT GGT TCT TGT GT-3' (FRAG. NO:1069) (SEQ ID NO:10446)  
 5'-TGG GGG TCC CTT TTT GGG CCT GTT GT-3' (FRAG. NO:1070) (SEQ ID NO:10447)  
 5'-GGC GTG GCT TGT GTG TTC GGT TTC-3' (FRAG. NO:1071) (SEQ ID NO:10448)  
 5'-TGC CCT GTC CTC CGG CGT CCC-3' (FRAG. NO:1072) (SEQ ID NO:10449)  
 5'- CGB BGC CTC CCC GGG GCB GGB TGB CTT TTG BGG GGC BCB CBG BTG TCT GGG CBT TGC CBG GTC CTG GGB BCB GBG  
 55 CCC CGB GCB GGB CCB GGB GTG CCG GCB GCG CGG GCC GGG GGC TGC TGG GBG CCB TBG CGB GGC TGB G-3' (FRAG.  
 NO:1073) (SEQ ID NO:10450)

#### Human Vascular Cell Adhesion Molecule 1 (VCAM-1)

##### Nucleic Acid and Oligonucleotide Fragments

- 60 5'-CCT CTT TTC TGT TTT TCC C CTC TGC CTT TGT TTG GGT TCG CTT CCT TTC TGC TTC TTC C CTG TGT CTC CTG TCT CCG  
 CTT TTT TCT TC GTC TTT GTT GTT TTC TCT TCC TTG CTG BGC BBG BTB TCT BGB TTC TGG GGT GGT CTC GBT TTT BBBB  
 GCT TGB GBB GCT GCB BBC BTT BTC CBB BGT BTB TTT GBG GCT CCB BGG BTC BCG BCC BTC TTC CCB GGC BTT TTB BGT  
 TGC TGT CGT-3' (FRAG.NO:1735) (SEQ ID NO:11117)  
 5'-C TGT CGT-3' (FRAG. NO:1736) (SEQ ID NO:11118)  
 5'-TGC TTC TTC C-3' (FRAG. NO:1737) (SEQ ID NO:11119)  
 65 H5VCAM1AS1: 5'-CCT CTT TTC TGT TTT TCC C-3' (FRAG. NO:1074) (SEQ ID NO:10451)  
 H5VCAM1AS2: 5'-CTC TGC CTT TGT TTG GGT TCG-3' (FRAG. NO:1075) (SEQ ID NO:10452)  
 H5VCAM1AS3: 5'-CTT CCT TTC TGC TTC TTC C-3' (FRAG. NO:1076) (SEQ ID NO:10453)  
 H5VCAM1AS4: 5'-CTG TGT CTC CTG TCT CCG CTT TTT TCT TC-3' (FRAG. NO:1077) (SEQ ID NO:10454)  
 H5VCAM1AS5: 5'-GTC TTT GTT GTT TTC TCT TCC TTG-3' (FRAG. NO:1078) (SEQ ID NO:10455)  
 70 CTG BGC BBG BTB TCT BGB TTC TGG GGT GGT CTC GBT TTT BBBB GCT TGB GBB GCT GCB BBC BTT BTC CBB BGT BTB TTT  
 GBG GCT CCB BGG BTC BCG BCC BTC TTC CCB GGC BTT TTB BGT TGC TGT CGT (FRAG. NO:1079) (SEQ ID NO:10456)

#### Human Endothelial Leukocyte Adhesion Molecule (ELAM-1)

##### Nucleic Acid and Antisense Oligonucleotide Fragments

5'-BBG TGB GBG CTG BGB GBB BCT GTG BBG CBB TCB TGB CTT CBB GBG TTC TTT TCB CCC GTT CTT GGC TTC TTC TGT C  
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 GTT CTT GGC TTC TGT TGT CCG T TGG CTT CTC GTT GTC CC TGT GGG CTT CTC GTT GTC CC CCC TTC GGG GGC TGG TGG  
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AGGGGAGTGG GACAACGAGA AGCCACATG TGAAGCTGTG AGATGCGATG CTGTCCACCA GCCCCGAGG GGTTTGGTGA  
45 GGTGTGCTCA TTCCCCTATT GGAGAATTCA CCTACAAGTC CTCTGTGCTC TTCAGTCTGT AGGAGGGATT TGAATTATAT  
GGATCAACTC AACTGTAGTG CACATCTCAG GGACAAGTGA CAGAAGAGGT TCCTTCTGTC CAAAGTGGTA AATGTTCAAG  
CCTGGCAGTT CCGGGAAGA TCAACATGAG CTGCAAGTGG GAGCCCGTGT TTGGCACTGT GTGCAAGTTC GCCTGTCTG  
AAGGATGGAC GCTCAATGGC TCTGCAGTCT GGACATGTGG AGCCACAGGA CACTGGTCTG GCCTGTCTAC TACCTGTGAA  
GCTCCCACTG AGTCAACAT TCCCTTGGTA CTGTGAGATT CTGTGCTGG ACTTCCCTC CTGACATTAG CACCATTTCT  
50 CCTCTGGCTT CGGAAATGCT TACGGAAAGC AAAGAAATTT GTTCTGCCA GCAGCTGCCA AAGCCTTGA TCAGACGGAA  
GCTACAAAA GCCTTCTTAC ATCCTTTAAG TTCAAAGAA TCAGAAACAG GTGCATCTGG GGAAGTAGAG GGATACACTG  
AAGTTAACAG AGACAGATAA CTCTCTCGG GTCTCTGGCC CTCTTCTGCT ACTATGCCAG ATGCCCTTAT GGGTGAAACC  
GCAACACCCA TCAACACTTC AATAGATCAA AGTCCAGCAG GCAAGGACCG CCTTCAACTG AAAAGACTCA GTGTTCCCTT  
TCTACTCTC AGGATCAAGA AAGTGTGGC TAATGAAGGG AAAGGATATT TTCTTCCAAG CAAAGGTGAA GAGACCAAGA  
55 CTCTGAAATC TCAGAATTCC TTTCTAACT CTCCCTTGT CGCTGTAAAA TCTTGGCACA GAAACACAAT ATTTTGTGGC  
TTTCTTCTT TTGCCCTTCA CAGTGTTTCG ACAGCTGATT ACACAGTTGC TGTCTAAGA ATGAATAATA ATTATCCAGA  
GTTTAGAGGA AAAAAATGAC TAAAAATATT ATAACCTTAA AAAATGACAG ATGTTGAATG CCCACAGGCA AATGCATGGA  
GGGTGTGTTA TGGTGCAAT CCTACTGAAT GCTCTGTGCG AGGGTTACTA TGCACAATTT AATCACTTTC ATCCCTATGG  
60 GATTCAGTGC TTCTTAAAGA GTTCTTAAAG ATTGTGATAT TTTTACTTGC ATTGAATATA TTATAATCTT CCATCTTCT  
TCATTCAATA CAAGTGTGGT AGGGACTTAA AAAACTTGTA AATGCTGTCA ACTATGATAT GGTAAAAAGTT ACTTATCTTA  
GATTACCCCT TCATTGTTTA TTAACAAATT ATGTTACATC TGTTTTAAAT TTATTTCAA AAGGAAACT ATTTGCTCCCT  
AGCAAGGCAT GATGTTAACC AGAATAAAGT TCTGAGTGT TTTACTACAG TTGTTTTTGG AAAACATGGT AGAATTGGAG  
AGTAAAAACT GAATGGAAGG TTGTATATT GTGAGATATT TTTTCAGAAA TATGTGGTTC CCACGATGAA AAACCTTCCAT  
GAGGCCAAAC GTTTTGAAC AATAAAAGCA TAAATGCAAA CACACAAAGG TATAATTTTA TGAATGTCTT TGTGGAAAA  
65 GAATACAGAA AGATGGATGT GCTTTGCATT CCTACAAAGA TGTGTTGTCAG ATGTGATATG TAAACATAAT TCTTGTATAT  
TATGGAAGAT TTAAATTC AATAGAAAC TCACCATGTA AAAGAGTCAT CTGGTAGATT TTTAAGCAAT TTTAAGCAAT GAAGATGTCT  
AATAGTTATT CCCTATTGTT TTCTTCTGT ATGTTAGGCT GCTCTGGAAG AGAGGAATGC CTGTGTGAGC AAGCATTTAT  
GTTTATTAT AAGCAGATTT AACAATTCCA AAGGAATCTC CAGTTTTCAG TTGATCACTG GCAATGAAAA ATTCAGTCT  
70 AGTAATTGCC AAAGCTGCTC TAGCCTTGAG GAGTGTGAGA ATCAAAATCT TCCTACACTT CCATTAACCT AGCATGTGTT  
GAAAAAAG GTTTCAGAGA AGTCTGGCT GAACACTGGC AACGACAAAG CCAACAGTCA AAACAGAGAT GTGATAAGGA  
TCAGAACAGC AGAGGTTCTT TTAAAGGGGC AGAAAAACTC AAGAAATAA GAGAGAACAA CTACTGTGAT CAGGCTATGT  
ATGGAATACA GTGTTATTTT CTTTGAAATT GTTAAAGTGT TGTAATATT TATGTAAACT GCATTAGAAA TTAGCTGTGT  
GAAATACCAG TGTGTTTGT GTTTGAGTTT TATTGAGAA TTTAAATTAT AACTTAAAT ATTTTATAAT TTTTAAAGTA  
TATATTATT TAAGCTTATG TCAGACCTAT TTGACATAAC ACTATAAAGG TTGACAATAA ATGTGCTTAT GTTT;  
75 3'(FRAG.NO.)(SEQ ID NO:11848)

5'-CCT TGC CTG CTG G-3' (FRAG. NO: 1739) (SEQ ID NO:11121)  
 5'-GTT GTC CC-3' (FRAG. NO: 1740) (SEQ ID NO:11122)  
 5'-GTT CTT GGC TTC TTC TGT C-3' (FRAG. NO:1080) (SEQ ID NO:10457)  
 5'-GGC TGG TGG-3' (FRAG. NO:1083) (SEQ ID NO:10461)  
 5'-CGT TGG CTT CTC GTT GTC CC-3' (FRAG. NO:1081) (SEQ ID NO:10458)  
 5'-TGT GGG CTT CTC GTT GTC CC-3' (FRAG. NO:1082) (SEQ ID NO:10459)  
 5'-CCC TTC GGG GGC TGG TGG-3' (FRAG. NO:1083) (SEQ ID NO:10460)  
 5'-GGC CGT CCT TGC CTG CTG G-3' (FRAG. NO:1084) (SEQ ID NO:10462)

#### **Human P Selectin Fragments**

5'-TTT TCT CTT TCG CTT TCT TTT CGT CTC CTG TTC CTC CTT TT TTG CTG TTT TTT CTC CTT CTT CTC TCC TTT CTT TTC-3' (FRAG. NO: 1741) (SEQ ID NO:11123)  
 5'-TCC TTT CTT TTC-3' (FRAG. NO: 1742) (SEQ ID NO:11124)  
 5'-CTC CTT TT-3' (FRAG. NO:1743) (SEQ ID NO:11125)  
 5'-TTT TCT CTT TCG CTT TCT TTT CGT CTC CTG TTC CTC CTT TT-3' (FRAG. NO:1085) (SEQ ID NO:10463)  
 5'-TTG CTG TTT TTT CTC CTT CTT CTC TCC TTT CTT TTC-3' (FRAG. NO:1086) (SEQ ID NO:10464)

#### **Human Endothelial Monocyte Activating Factor**

##### **Nucleic Acid & Antisense Oligonucleotide Fragments**

5'-TTT TCT CTT TCG CTT TCT TTT CGT CTC CTG TTC CTC CTT TT TTG CTG TTT TTT CTC CTT CTT CTC TCC TTT CTT TTC-3' (FRAG. NO: 1744) (SEQ ID NO:11126)  
 5'-CC TTT CTT TTC (FRAG. NO: 1745) (SEQ ID NO:11127)  
 5'-CTG TTC CTC CTT TT-3' (FRAG. NO:1746) (SEQ ID NO:11128)  
 5'-TTT TCT CTT TCG CTT TCT TTT CGT CTC CTG TTC CTC CTT TT-3' (FRAG. NO:1087) (SEQ ID NO:10465)  
 5'-TTG CTG TTT TTT CTC CTT CTT CTC TCC TTT CTT TTC-3' (FRAG. NO:1088) (SEQ ID NO:10466)

#### **Human IL3 Nucleic Acid and Antisense Oligonucleotide Fragments**

5'-CTC TGT CTT GTT CTG GTC CTT CGT GGG GCT CTG TGT CGC GTG G GTG CGG CCG TGG CC GGC GGB CCB GGB GTT GGB GCB GGB GCB GCB CGG GCB GGC GGC TCB TGT TTG GBT CGG CBG GBG GCB CTC (FRAG. NO: 1747) (SEQ ID NO:11129)]  
 5'-G GBG GCB CTC-3' (FRAG. NO: 1748) (SEQ ID NO:11130)  
 5'-GT GGG GCT CTG-3' (FRAG. NO:1749) (SEQ ID NO:11131)  
 HUMIL3AAS1: 5'-CTC TGT CTT GTT CTG GTC CTT CGT GGG GCT CTG-3' (FRAG. NO:1089) (SEQ ID NO:10467)  
 HUMIL3AAS2: 5'-TGT CGC GTG G GTG CGG CCG TGG CC-3' (FRAG. NO:1090) (SEQ ID NO:10468)  
 GGC GGB CCB GGB GGB GCB GGB GCB CGG GCB GGC GGC TCB TGT TTG GBT CGG CBG GBG GCB CTC (FRAG. NO:1091) (SEQ ID NO:10469)

#### **Human IL3 Receptor Nucleic Acid and Antisense Oligonucleotide Fragments**

5'-TCT GGG GTG TCC TGG CCT TCG TGG TTC CTC TTT CGT TTG CCG TCC GCG GGG GCC CCC GGG CCT GGC TGC GCT CCT GCC CCG CTT TCC CGG GCT CTT GCG CTG GGG GGT GCT CC CGT GTG TTT GCG CCC TC CTC CTG GTC GCG CTT GTG GTT TGG GGG CCG GCT TTG CCC GCC TCC CGG CGC CTG GCC CGG CC TTC CTG GGC TGC GTG CGC GTT CTG TTC TTC TTC CTG GCT CTG GGG TGT CCT GGC CTT CGT GGT TCC TCT TCC TTC GTT TGC CGT CCG CGG GGG CCC CCG GGC CT GGC TGC GCT CCT GCC CCG CTT TCC CGG GCT CTT GCG CTG GGG GGT GCT CCC GTG TGT TTG CGC CCT CCT GGT CGC GCT TGT CGT TTT GG GGC CGG CTT TGC CCG CCT CCC GGC GCC TGG CCC GGC CTT CCT GGG CTG CGT GCG CGT TCT GTT CTT CTT CCT GGC GCA GGA GAC AGG GCA GGG CGA TCA GGA GCA GCG TGA GCC AAA GGA GGA CCA TCG GGA ACG CAG CTC CGG AAC GCA GGA CAG AGG TGC C GC BGG BGB CBG GGC BGG GCG BTC BGG BGC BGC GTG BGC CBB BGG BGG BCC BTC GGG BBC GCB GCT CCG GBB CGC BGG BCB GBG GTG CC-3' (FRAG. NO: 1750) (SEQ ID NO:11132)  
 GBG GTG CC-3' (FRAG. NO: 1751) (SEQ ID NO:11133)  
 5'-GCC CCG C-3' (FRAG. NO:1752) (SEQ ID NO:11134)  
 5'-TCTGGGGTGTCTCTG (FRAG. NO:1092) (SEQ ID NO:10470)  
 5'-GCCCTTCGTGGTTCC (FRAG. NO:1093) (SEQ ID NO:10471)  
 5'-TCTTCTTCGTTTGC (FRAG. NO:1094) (SEQ ID NO:10472)  
 5'-CGTCCGCGGGGCCCCCGGGCCT (FRAG. NO:1095) (SEQ ID NO:10474)  
 5'-GGC TGC GCT CCT GCC CCG C (FRAG. NO:1096) (SEQ ID NO:10473)  
 5'-CTCTTTCCCGGGCTCTT (FRAG. NO:1097) (SEQ ID NO:10475)  
 5'-GCGCTGGGGGTGCTCC (FRAG. NO:1098) (SEQ ID NO:10476)  
 5'-CGTGTGTTTTCGCGCCCTCCTCTGGTCGC (FRAG. NO:1099) (SEQ ID NO:10477)  
 5'-GCTTGTGCTTTTGG (FRAG. NO:1100) (SEQ ID NO:10478)  
 5'-GGCCGGCTTTGCCCGCTCCC (FRAG. NO:1101) (SEQ ID NO:10479)  
 5'-GGCGCCTGGCCCGGCC (FRAG. NO:1102) (SEQ ID NO:10480)  
 5'-TTCTGGGCTGCGTGC (FRAG. NO:1103) (SEQ ID NO:10481)  
 5'-GTTCTGTTCTTCTCTCTGGC (FRAG. NO:1104) (SEQ ID NO:10482)  
 5'-GCB GGB GCB BGG GCB GGG CGB TCB GGB GCB GCG TGB GCC BBB GGB GGB CCB TCG GGB BCG CBG CTC CGG BBC GCB GGB 5'-CBG BGG TGC C (FRAG. NO:1105) (SEQ ID NO:12488)

#### **Human IL-4 Nucleic Acid and Antisense Oligonucleotide Fragments**

5'-CTC TGG TTG GCT TCC TTC GCC GGC BCB TGC TBG CBG GBB GBB CBG BGG GGG BBG CBG TTG GGB GGT GBG BCC CBT TBB TBG GTG TCG B-3' (FRAG. NO: 1753) (SEQ ID NO:11135)  
 5'-GCC GGC BCB-3' (FRAG. NO: 1754) (SEQ ID NO:11136)  
 5'-T TCC TTC-3' (FRAG. NO:1755) (SEQ ID NO:11137)  
 5'-CTC TGG TTG GCT TCC TTC-3' (FRAG. NO:1106) (SEQ ID NO:10484)  
 5'-GCCGCBCTGTGCBGGBBGBBGBGGGGGGBGCBGTTGGGCGGTGGBGCCBTTBBTGGTGTGCB-3' (FRAG. NO:1107) (SEQ ID NO:10485)

#### **Human IL4 Receptor Nucleic Acid and Antisense Oligonucleotide Fragment**

5'-TCT GCC CTG TCC GCC GGC TCT TCG GTG GCT CGG CCC CGC TCC TTG TCT TGC CGC GGG TTG GTT CCT GGG CCT GGT TCT TGC GGC COT TTT GGT CTG CTG GCT GGT GCG CCG CGG TGC GGC GGG TGG CTT GCT GTT CTG CCT GGG CTC TCC CCT CTC CTC CTT TTC TCC CTT CCT CTG TCT TGC CTC CTT CCT CTG GGT CCT CTT GGC CTG GGC GCT CTT CCC CTC GGG CGG CTG CGG GCG CTC GTG CTG CCT GGT CCG CTC CCT GGG GGT GCT CCT TCC CTT TCC CCG CTC GTG GGG TTT GCG GGG CTG GGC TGC CCT GGG GGG TCT GGG CCT TTT GGG GTC GGC TGG CTG CTG CTT CGG GCC GCC TGG GCT TCC CTG TGC CCC

- TTT CCT CTG CTG GGT CCC CCT CCC GTT CCA AGC TGC ACC GCA CAG ACC GGC GCT ACA GGA CAG AGC CAG GCA AGC  
ACC CAT GGG GAT CCA GGC CCA GCT GTT CCB BGC TGC BCC GCB CBG BCC GGC GCT BCB GGB CBG BGC CBG GCB BGC  
BCC CBT GGG GBT CCB GGC CCB GCT G -3'(FRAG. NO: 1756)(SEQ ID NO:11138)
- 5 5'-TCTGCGC-3' (FRAG. NO: 1757) (SEQ ID NO:11139)  
5'-CCT GCT CCT GGG G (FRAG. NO:1758) (SEQ ID NO:11140)  
5'-TCTGCGCGCCCTGCTCC (FRAG. NO:1108) (SEQ ID NO:10486)  
5'-CGCCCGGCTTCTCT (FRAG. NO:1109) (SEQ ID NO:10487)  
5'-CGTGTGGGCTTCGG (FRAG. NO:1110) (SEQ ID NO:10488)  
5'-CCCCGCGCCTCCGTTGTTCTC (FRAG. NO:1111) (SEQ ID NO:10489)
- 10 5'-TGCTCGCTGGGCTTG (FRAG. NO:1112) (SEQ ID NO:10490)  
5'-GGTTTCTCTGGGGCCCTGGGTTTC (FRAG. NO:1113) (SEQ ID NO:10491)  
5'-TCTGCCGGGCTCGTTTC (FRAG. NO:1114) (SEQ ID NO:10492)  
5'-GGGTGCTGGGCTGCG (FRAG. NO:1115) (SEQ ID NO:10493)  
5'-CTTGGTGTCTGGGGCTCC (FRAG. NO:1116) (SEQ ID NO:10494)
- 15 5'-GGCGGCTGCGGGCTGGGTTGGG (FRAG. NO:1117) (SEQ ID NO:10495)  
5'-CTTGGCTGGTTCCTGGCCTCGGG (FRAG. NO:1118) (SEQ ID NO:10496)  
5'-CCTCCTCCTCCTCCTCGCTCCCTTTTCTTCTCT (FRAG. NO:1119) (SEQ ID NO:10497)  
5'-TCCCTGCTGCTCTC (FRAG. NO:1120) (SEQ ID NO:10498)  
5'-TGCCCTCCCTTCCCTCCTGG (FRAG. NO:1121) (SEQ ID NO:10499)  
5'-GGTGCCTCCTTGGGCCCTGC (FRAG. NO:1122) (SEQ ID NO:10500)
- 20 5'-GGCTGCTCCTTGCCCC (FRAG. NO:1123) (SEQ ID NO:10501)  
5'-CTCTGGGTGCGGCTGGC (FRAG. NO:1124) (SEQ ID NO:10502)  
5'-GGGGCGTCTCTGTGC (FRAG. NO:1125) (SEQ ID NO:10503)  
5'-CTGGCCTGGGTGCC (FRAG. NO:1126) (SEQ ID NO:10504)
- 25 5'-GCTCTCCTGGGGGGGTGGCTCCCTGTCC (FRAG. NO:1127) (SEQ ID NO:10505)  
5'-CCTTTTCCCCCGGCTCC (FRAG. NO:1128) (SEQ ID NO:10506)  
5'-GTGGGGGCTTTGGC (FRAG. NO:1129) (SEQ ID NO:10507)  
5'-GGG GGT CTG TGG CCT GCT CCT GGG G (FRAG. NO:1130) (SEQ ID NO:10508)  
5'-AGGGGTCTGGGGCCCTC (FRAG. NO:1131) (SEQ ID NO:10509)
- 30 5'-TTTGGGGGTCTGGCTTG (FRAG. NO:1132) (SEQ ID NO:10510)  
5'-GCTGCTGCTGCTTCC (FRAG. NO:1133) (SEQ ID NO:10511)  
5'-GGGGCCTGCCGTGGGGC (FRAG. NO:1134) (SEQ ID NO:10512)  
5'-TGCTCTCTGTGTGCTCCCTT (FRAG. NO:1135) (SEQ ID NO:10513)  
5'-TGCTGCTGTCTGG (FRAG. NO:1136) (SEQ ID NO:10514)
- 35 5'-GGTTCCCGCCTTCCT (FRAG. NO:1137) (SEQ ID NO:10515)  
5'-GTT CCC AGA GCT TGC CAC CTG CAG CAG GAC CAG GCA GCT CAC AGG GAA CAG GAG CCC AGA GCA AAG CCA CCC CAT  
TGG GAG ATG CCA AGG CAC CAG GCT G (FRAG. NO:1138) (SEQ ID NO:10516)  
5'-GTT CCC BGB GCT TGC CBC CTG CBG CBG GBC CBG GCB GCT CBC BGG GBB CBG GBG CCC BGB GCB BBG CCB CCC CBT  
TGG GBG BTG CCB BGG CBC CBG GCT G-3' (FRAG. NO:1139) (SEQ ID NO:10517)
- 40 **Human IL5 Nucleic Acid and Antisense Oligonucleotide Fragments**  
5'-TCCCTGTTTCCCCTTTTCG TTCTGCGTTT GCCTTTGGCG TTTTGTGT GTTTCTCTC TCCGTCTTC TTCTCCCT  
GTGGGBBTTT CTGTGGGBT GGCBTBCBG TBGGCBGCTC CBBGBGCTBG CBBBCTCBBB TGCBBBGBB TCCTCBTGGC  
TCTGBBBCCG TGGGAATTTC TGTGGGBTG GCATACACGT AGGCAGCTCC AAGAGCTAGC AAACCTCAAAT GCAGAAGCATC  
CTCATGGCTC TGAAACG-3' (FRAG. NO: 1759) (SEQ ID NO:11141)
- 45 5'-GCC CCG GG-3' (FRAG. NO: 1760) (SEQ ID NO:11142)  
5'-G GGT TTC T-3' (FRAG. NO: 1761) (SEQ ID NO:11143)  
5'-GTG GGG BTG GC-3' (FRAG. NO: 1762) (SEQ ID NO:11144)  
5'-CCB BGB GCT BGC-3' (FRAG. NO: 1763) (SEQ ID NO:11145)  
5'-TCC CTG TTT CCC CCC TTT-3' (FRAG. NO:1140) (SEQ ID NO:10518)
- 50 5'-CGT TCT GCG TTT GCC TTT GGC-3' (FRAG. NO:1141)(SEQ ID NO:10519)  
5'-GTT TTT TGT TTG TTT TCT-3' (FRAG. NO:1142)(SEQ ID NO:10520)  
5'-CTC TCC GTC TTT CTT CTC C-3' (FRAG. NO:1143) (SEQ ID NO:10521)  
5'-CCT CCT GCC TGT GTC CCT GCT CCC C-3' (FRAG. NO:1144) (SEQ ID NO:10522)  
5'-GAG GGT TTC TGG CTT CCT CTC T-3' (FRAG. NO:1145) (SEQ ID NO:10523)
- 55 5'-TGT CTC TCT GTC CTT TTG TT-3' (FRAG. NO:1146) (SEQ ID NO:10524)  
5'-TGT TGT GCG GCC TGG TGC TGC CCT GCC CCG GG-3' (FRAG. NO:1147) (SEQ ID NO:10525)  
5'-GTG GGA ATT TCT GTG GGG BTG GCA TAC ACG TAG GCA GCT CCA AGA GCT AGC AAA CTC AAA TGC AGA AGC ATC CTC  
ATG GCT CTG AAA CG-3' (FRAG. NO: 1764) (SEQ ID NO:11146)  
5'-GTG GGB BTT TCT GTG GGG BTG GCB TBC BCG TBG GCB GCT CCB BGB GCT BGC BBB CTC BBB TGC BGB BGC BTC CTC  
BTG GCT CTG BBB CG-3' (FRAG. NO:1148) (SEQ ID NO:10526)
- 60 **Human IL-5 Receptor Nucleic Acid and Antisense Oligonucleotide Fragments**  
5'-CTCAGTGGCC CCCAAAAGGA TGAGTAATAC ATGCGCCACG ATGATCATAT CCTTTTACT ATGAGGCCGT GTCTGTCGTG  
TCTTTCCTTT GCTCTTGGTG TGTCTTTGCT GTGCCCTGCC TCTCTGCCG TGTCTGTCGT GTCTTTCCTT TGCTCTTGGT  
GTGTCCTTGC TGTGCCCTGC CTCCTGCC CGTGTCTGTC GTGTCTTCC TTGCTCTTG GTGTGTCTTT GCTGTGCCCT  
GCCTCTCTGC-3' (FRAG. NO: 1765) (SEQ ID NO:11147)
- 65 5'-CCG TGT C-3' (FRAG. NO: 1766) (SEQ ID NO:11148)  
5'-GCCCTGCC-3' (FRAG. NO: 1767) (SEQ ID NO:11149)  
5'-CCG TGT CTG TCG TGT CT-3' (FRAG. NO:1149) (SEQ ID NO:10527)  
5'-TTCCTTTGCTCTTG-3' (FRAG. NO:1150) (SEQ ID NO:10528)
- 70 5'-GTGTGTCTTTGCTGT-3' (FRAG. NO:1151) (SEQ ID NO:10529)  
5'-GCCCTGCCCTCTGTC-3' (FRAG. NO:1152) (SEQ ID NO:10530)  
5'-CT CBGTGGCCCC CBBBGGBTG BGTBBTBCBT GCGCCBCGT GBTCBTBTCC TTTTBTCTBT BGGB (FRAG. NO: 1768) (SEQ  
ID NO:11150)

**Human IL-6 Receptor Fragments**

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5'-CTCCTGGGGG TBCTGGGGCB GGGBBGGCBG CBGGCBBCBC CBGGBCBGC CCCBGGGBG BGGCBCTGG BCCGBBGGCG  
CTTGTGGGBG BGGBTTCBT BGCTGGGCTC CTGGBGGGBG GBTBGGC-3'(FRAG.NO:1777)(SEQ ID NO:11159)

#### **Human Monocyte-derived Neutrophil Chemotactic Factor**

##### **Nucleic Acid and Antisense Oligonucleotide Fragments**

- 5 5'-GGGGTGGBBB GCTTTGGBGT BTGTCTTTBT GCBCTGBCBT CTBBGTTCCT TBGCBCTCCT TGGCBBBCT GCBCTTCBC  
BCBGBGCTGC BGGBTTCBG BGGCTGCCB BGGGBGCCB GGCBCGCTTG GBBGTCTGT TTBCBCBCB TGBGTGGTT  
CCTCCGGGC TTGTGTCTC TGCTGTCTT TGGTCTTC CGTGGTTT TCCTGGCTC TTGCTCTTC TCTGG CCCT TGGC-3'  
(FRAG. NO:1778) (SEQ ID NO:11160)
- 5'-GGBGT BTG-3' (FRAG. NO:1779) (SEQ ID NO:11161)
- 10 5'-GCBCTGBCBT CT-3' (FRAG. NO:1780) (SEQ ID NO:11162)
- 5'-CCG GTG G-3' (FRAG. NO:1781) (SEQ ID NO:11163)
- 5'-GG CCC TTG GC-3' (FRAG. NO:1782) (SEQ ID NO:11164)
- 5'-GCT TGT GTG CTC TGC TGT CTC T-3' (FRAG. NO:1192) (SEQ ID NO:10570)
- 5'-TGG TTC CTT CCG GTG GTT TCT TCC TGG CTC TTG TCC T-3' (FRAG. NO:1193) (SEQ ID NO:10571)
- 15 5'-TTC TCT TGG CCC TTG GC-3' (FRAG. NO:1194) (SEQ ID NO:10572)
- 5'-GGGGTGGBBB GCTTTGGBGT BTGTCTTTBT GCBCTGBCBT CTBBGTTCCT TBGCBCTCCT TGGCBBBCT GCBCTTCBC  
BCBGBGC-3' (FRAG. NO:1783) (SEQ ID NO:11165)

##### **Human Neutrophil Elastase (Medullasin) Nucleic Acid and Antisense Oligonucleotide Fragments**

- 20 5'-GGGCTCCCGC CGCGBGGGT TBGGGGTCC CBGGBCBCC CGBCCGCGC GGBCGTTTBC BTTCGCCBCG CBGTGCGCGG  
CCGBCBTGBC GBBGTTGGGC GCBTTCBGGG TGGCGCCGC BGGTGGCCT CCGCGCBGCT GCBGGBCBCB CBTGBBGGG  
CBCGCGTGGG GCGCGCTCG CCGGCCCGCC BCBTCTCCG BGGCBGCGC GGTGCCCCC BGCBCBBGG CCGCBGGBC  
BCBGGCCBGG BGCBCGCGB GTCGCGGCC GBGGTCTGT GTGGGCTGG GGCTCCGGG TCTCTGCCC TCCGTGCTGG  
TGGGGCTGGG GCTCCGGG TCTCTGCCCC TCCGTGCCG GTGGGCGCG GCTCGCCGC CCCCCCTGC CCGGTGGGCT  
CCCCCGCGC GCGGCTCG CCGCCCTCG TGGTCTCTG TGGCCGGTC CCGGTCCCG GGTGGGGCG CBGTGCGCG
- 25 GCGBGGGTCT-3' (FRAG. NO:1784) (SEQ ID NO:11166)
- 5'-GG TGG GGC-3' (FRAG. NO:1785) (SEQ ID NO:11167)
- 5'-G GGG CCG -3' (FRAG. NO:1786) (SEQ ID NO:11168)
- 5'-GGC CGG GTC CGG G-3' (FRAG. NO:1787) (SEQ ID NO:11169)
- 5'-TGG TGG GGC TGG GGC TCC GGG GTC TCT GCC CCT CCG TGC-3' (FRAG. NO:1195) (SEQ ID NO:10573)
- 30 5'-CGC GTG GGG CCG CGC TCG CCG GCC CCC C-3' (FRAG. NO:1196) (SEQ ID NO:10574)
- 5'-CCT GCC GGG TGG GCT CCC GCC GCG-3' (FRAG. NO:1197) (SEQ ID NO:10575)
- 5'-CGC CGG CCT GCC GGC CCC TC-3' (FRAG. NO:1198) (SEQ ID NO:10576)
- 5'-GTG GGT CCT GCT GGC CGG GTC CCG GGG GTG GGG-3' (FRAG. NO:1199) (SEQ ID NO:10577)
- 5'-CGG GTC TCG GCG GCC GGG GGT C-3' (FRAG. NO:1200) (SEQ ID NO:10578)
- 35 5'-GGGCTCCCGC CGCGBGGGT TBGGGGTCC CBGGBCBCC CGBCCGCGC GGBCGTTTBC BTTCGCCBCG CBGTGCGCGG  
CCGBCBTGBC GBBGTTGGGC GCBTTCBGGG TGGCGCCGC BGGTGGCCT CCGCGCBGCT GCBGGBCBCB CBTGBBGGG  
CBCGCGTGGG GCGCGCTCG CCGGCCCGCC BCBTCTCCG BGGCBGCGC GGTGCCCCC BGCBCBBGG CCGCBGGBC  
BCBGGCGBGG BGCBCGCGB GTCGCGGCC GBGGTCTGT GTGGGCTGG GGCTCCGGG TCTCTGCCCC TCCGTGC-3'  
(FRAG. NO:1788) (SEQ ID NO:11170)

##### **Human Neutrophil Oxidase Factor Nucleic Acid and Antisense Oligonucleotide Fragments**

- 40 5'-CGGGBGTGGG GGTCTGGBC GGCCTGGBG GCBTCCBGGG CTCCTTCCB GTCCTTCTG TCCGCTGCCB GCBCCCTTC  
BTTCBGGG CTGTTGGCCT CCBCBGGGB CBGTBTBGG TBGBBCTBG BGGGCCGCC TCCBCBGGG BCBTGGTCTT  
TCTTTCGC TGCTCTCTG GGGTTTTCG TCTGGGTGGG CTTCCTCTT GGGGCTGCTG CTGGGCTCTT CTTTGTGTT  
CTGGCTGCT GCTCTCTG GCCCTTCC TGGGTGTCT TGTTTGTG GCCTCCBCCB GGBCBTG-3' (FRAG. NO:1789) (SEQ  
ID NO:11171)
- 5'-CGGGBGTGGG GG-3' (FRAG. NO:1790) (SEQ ID NO:11172)
- 5'-GCCBGCBCCC-3' (FRAG. NO:1791) (SEQ ID NO:11173)
- 5'-C CBC CBG-3' (FRAG. NO:1792) (SEQ ID NO:11174)
- 5'-GGC CTC CBC CBG GGB CBT G-3' (FRAG. NO:1201) (SEQ ID NO:10579)
- 50 5'-GCT CTT CTT GTC CGC TGC C-3' (FRAG. NO:1202) (SEQ ID NO:10580)
- 5'-TCT CTG GGG TTT TCG GTC TGG GTG G-3' (FRAG. NO:1203) (SEQ ID NO:10581)
- 5'-GCT TTC CTC CTG GGG CTG CTG CTG-3' (FRAG. NO:1204) (SEQ ID NO:10582)
- 5'-GGC TCT TCT TTT TGT TTC TGG CCT GGT G-3' (FRAG. NO:1205) (SEQ ID NO:10583)
- 5'-CTC TCT CGT GCC CTT TCC-3' (FRAG. NO:1206) (SEQ ID NO:10584)
- 55 5'-CTT GGG TGT CTT GTT TTT GT-3' (FRAG. NO:1207) (SEQ ID NO:1216)
- 5'-GGC CTC CBC CBG GGB CBT G-3' (FRAG. NO:1208) (SEQ ID NO:10586)
- 5'-CGGGBGTGGG GGTCTGGBC GGCCTGGBG GCBTCCBGGG CTCCTTCCB GTCCTTCTG TCCGCTGCCB GCBCCCTTC  
BTTCBGGG CTGTTGGCCT CCBCBGGGB CBGTBTBGG TBGBBCTBG BGGGCC-3' (FRAG. NO:1793) (SEQ ID NO:11175)

##### **Human Cathepsin G Nucleic Acid and Antisense Oligonucleotide Fragments**

- 60 5'-CCCTCCBCT CTGCTCTGBC CTGCTGGBCT CTGGBTCTGB BGTBCCGCB TGTBGGGGC CTGCTCTCC  
GGCTCCGCT GBTCTCCCT GCCTCGCCC CBGTGGGTGB GBGBBGGCC BGCBBGGCB GGBGTGGCTG CBTCTTCTC  
GGTGGGGCT GCTCTCCCG CTCCGTGTG TTGCTGGGTG TTTCCCGTC TCTGGTCTG CTTCGGGGT CGT-3' (FRAG.  
NO:1794) (SEQ ID NO:11176)
- 5'-GBGBTBCGCC-3' (FRAG. NO:1795) (SEQ ID NO:11177)
- 65 5'-CBGCCCCBG-3' (FRAG. NO:1796) (SEQ ID NO:11178)
- 5'-TCC CGT CTC TGG-3' (FRAG. NO:1797) (SEQ ID NO:11179)
- 5'-GTG GGG CCT GCT CTC CCG GCC TCC G-3' (FRAG. NO:1209) (SEQ ID NO:10587)
- 5'-TGT GTT GCT GG GTG TTT TCC CGT CTC TGG-3' (FRAG. NO:1210) (SEQ ID NO:10588)
- 5'-TCT GCC TTC GGG GGT CGT-3' (FRAG. NO:1211) (SEQ ID NO:10589)
- 70 5'-CCCTCCBCT CTGCTCTGBC CTGCTGGBCT CTGGBTCTGB BGTBCCGCB TGTBGGGGC GGBGTGGGG CTGCTCTCC  
GGCTCCGCT GBTCTCCCT GCCTCGCCC CBGTGGGTGB GBGBBGGCC BGCBBGGCB GGBGTGGGTG-3' (FRAG. NO:1798)  
(SEQ ID NO:11180)

##### **Human Defensin 1 Nucleic Acid and Antisense Oligonucleotide Fragments**



5'-CCGGGGGCTGC BGCBBCTCB TCBGCTCTTG CCTGGGCTGG CTCBGCCTGG GCCTGCBGGG CCBCCBGGGB BBTGGCBGCB  
BGBBTGGCGB GGGTCTCTBT GGCTGGGGTC BCBGBTCCTC TBGCTBGGCB GGGTGBCCBG BGBGGGC GGG TCC TCB TGG CTG  
GGG GCC TGG GCC TGC BGG GCC GCT CTT GCC TGG BGT GGC TC GCC CBG BGT CTT CCC TGG T GCTCAGCCTC  
5 CAAGAGGACC AGCCTCTCCC CAGTCTCTGA AATCCTGAGT GTTGCCCTGCC AGTCGCCATG AGAACTTCCT ACCTTCTGCT  
GTTTACTCTC TGCTTACTTT TGCTGAGAT GGCTCAGGT GGTAACTTTC TCACAGGCCCT TGGCCACAGA TCTGATCATT  
ACAATTCGCT CAGCAGTGGA GGGCAATGTC TCTATTCTGC CTGCCGATC TTTACCAAAA TTCAAGGCAC CTGTTACAGA  
GGGAAGGCCA AGTGCTGCAA GTGAGCTGGG AGTGACCAGA AGAAATGACG CAGAAGTGAA ATGAACCTTT TATAAGCATT  
CTTTTAATAA AGGAAAATTG CTTTGAAGT AT CTGCAGTGGT AAAAAGATTTC TATATCTGCT GTTTGATGAA TGCAGCACCC  
10 ACTAGCCACA TAGTGCTCGT GAGCACITGC AATGCGGCTA GGGTGATTTC AATTAACCTA AAAGAGAACA GCCACAGGGA  
GCATGTGGCT GCCATATTGG ATGGTGCTGC TTTGAGAACA AATGAGAGA AATGAAGCCT CTATTTACCT TGGTTGGCGG  
AACACATTGA AGGACTCTG TATTGATACC AGGCTTCAA CTTTGGGAAG TGTACTGGCC AACTTAAACA CATCCACAGG  
AGAATGAAGA GGTTTGGGAA GGGACCAGAA ACCAGGCATT GAGGACAATG AGAAGAGTTT TTCAAAAGTG GAATTACTGC  
AAAAAGTGGG AAAATAGCCT TTGGATGGAA GTTACTAGT AGACAATTTC CATCGGTGTG AAAGCCATCT TTCCAACAGA  
GATCTGCAAC ATGAGAATGT ACTGTCTCCT AGGGTAGCGA TGGCCTCTTG TATTAGTCCG CTCAGGCTAC CAGATTTATC  
15 GTTTAAACTG CCCATAAACA GACCAGGCAG TTTAAACAAC AGAAATTTAT TTCTCGCAG TCCTGGAGGC AGGAAGTCTG  
CGATGAGTGT GGAAGCAGGG TTGGCTTCTT CTCAGGTGTC TGTCCTTGGC TGGTAGATGA CCGCCGCTC CTGCGGTCTC  
CACATGGTCT TTCTCTGTG TGTGCTGTC CCAATCTCTT CTTATAAGGA TGCAAGTCTT ATGGATCAGA GACACCCCA  
ATGACCGTGT TTAACITGAA TCACCTCTTT AAAGTTTCTC TCTCAAATA CAATCACCTC CTGAGGCACT GTTAGGGCTT  
CGACACAGGA ATCTTTTCC TAGGGGATTC AGTTCAGTGC AAAACGCCTA CCAGTGGAGA CTTGCAACAT GGGCGCTGCT  
20 TGGTCCCTCG CCAGGAATAT CACAGGCGAC GTTCCCTGT TGCATGGAAT AGAAGGCTAT TCCAGAGTAC TGTCTTAT  
TATCAGATCT GGGATACTGG GAGAAGGGCA AAATAAAGTC CAAGTAGAAA AAAAAGCTAT GAAAGTTTGA GAGAGTAACC  
ATAATTTTCA CCGATGTGA AACGATCCTA GATTTAGCT GAAATAGTGA TGTGGGAAGT GAGGGGGCCG GGATTCAGG  
CAGAGGGAAC AGCGTAAGTG AAGGCATGGA AGGAGGGAAG TGTAGGCTGT GTTTGAAGAG TGGCAGCTGC TTCCACATT  
CTAAAACACA GGTATGTGATT TTGGGGTGTG TTGAGACAA GCAGAAAAC TGTTTGGAAA AATAACTGTA ATTCCCTGCA  
25 CATTTAAAT CTCTCAGCAG AAGAAAACCC CACTCAGAAC CCCACTGTTC ATTCTTGGC TTGATTTGG SCACAGTGG  
CATAGCCCCA GACTGAGTAA GCTCTTCA GACCTCATTT CATGAGTAGC CCCAAAGATC AATCATGGGC CAATTTCTTG  
GAAGACAGCA CTCTCCGGTG TTTGCACTT ATTTGCTCTG CTTTCCGAG ATGTTCTCAA ATCGTTGAGC CTACAAAGCCA  
TGAGTCTGAA GTGTTGTGT TCCCTCCTTA CAGGTGGTAA CTTTCTACA GGCCTTGGCC ACAGATCTGA TCATTACAAT  
TGCGTCAGCA GTGGAGGGCA ATGCTCTAT TCTGCCTGCC CGATCTTTAC CAAAATTCAA GGCACCTGTT ACAGAGGGAA  
30 GGCCAAGTGC TGCAAGTGAG CTGAGAGTGA CCAGAAGAAA TGACGCAGAA GTGAAATGAA CTTTATAA GCATTCITTT  
AATAAAGGAA AATTGCTTTT GAAGTATACC TCTTTGGGC CAAAATGAAT CTTGTGTCTC AATTGGAAGA GGTAAAGAAG  
TAGGGGGTTA GGGTGCATGG GTTGAACGT GAGACAGGTC GAACCACAAA GCCTGCCTGG AAAAGGGGAG TGACGCTCTA  
GGCTTCAGTG ATGTACCTC CACTTTGTTT GATCCACAAA CCAACAGGTG ACTGATTTTG GTCAGCTCAG CTCCTCAAAGG  
AGCCAGCCTC TCCCAGTTC CTGAAATCCT GAGTGTGTC TGCCAGTGC CATGAGAACT TCCTACCTTC TGCTGTTTAC  
35 TCTCTGCTTA CTTTGTCTG AGATGGCCTC AGGTGGTAACT TTCTCAGAG GCCTTGGCCA CAGATCTGAT CATTACAATT  
GCGTCAGCAG TGGAGGGCAA TGTCTCTATT CTGCCTGCC GATCTTTACC AAAATTCAA GACCTGTGA CAGAGGGAAG  
GCCAAGTGCT GCAAGTGAGC TGGAGTGAC CAGAAGAAAT GACGCAGAAG TGAAATGAAC TT -3' (FRAG.NO:1799) (SEQ ID  
NO:12379)  
5'-GTCAGCTCAG CCTCCAAAGG AGCCAGCCTC TCCCAAGTTC CTGAAATCCT GAGTGTGTC TGCCAGTGC CATGAGAACT  
40 TCCTACCTTC TGCTGTTTAC TCTCTGCTTA CTTTGTCTG AGATGGCCTC AGGTGGTAACT TTTCTCAGAG GCCTTGGCCA  
CAGATCTGAT CATTACAATT GCGTCAGCAG TGGAGGGCAA TGTCTCTATT CTGCCTGCC GATCTTTACC AAAATTCAA  
GCACCTGTTA CAGAGGGAAG GCCAAGTGCT GCAAGTGAGC TGGAGTGAC CAGAAGAAAT GACGCAGAAG TGAAATGAAC TT-  
3' (FRAG.NO: ) (SEQ ID NO:11844)  
5'-CTGCAGTGGT AAAAAGATTTC TATATCTGCT GTTTGATGAA TGCAGCACCC ACTAGCCACA TAGTGCTCGT GAGCACTTGC  
45 AATGCGGCTA GGGTGATTTC AATTAACCTA AAAGAGAACA GCCACAGGGA GCATGTGGCT GCCATATTGG ATGGTCTGTC  
TTTGAGACAA AATGAGAGA AATGAAGCCT CTATTTACCT TGGTTGGCGG AACACATTGA AGGGATCTG TATTGATACC  
AGGCTTCAA CTTTGGGAAG TGTACTGGCC AACTTAAACA CATCCACAGG AGAATGAAGA GGTTTGGGAA GGGACCAGAA  
ACCAGGCATT GAGGACAATG AGAAGAGTTT TTCAAAAGTG GAATTACTGC AAAAAGTGA AAAAAGCTC TTGGATGGAA  
GTTACTGATG AGACAATTTC CATCGGTGTG AAAGCCATCT TTCCAACAGA GATCTGCAAC ATGAGAATGT ACTGCTCTC  
50 AGGGTAGCGA TGGCCTCTTG TATTAGTCCG CTCAGGCTAC CAGATTTATC GTTTAAACTG CCCATAAACA GACCAGGCAG  
TTTAAACAAC AGAAATTTAT TTCTCGCAG TCCTGGAGGC AGGAAGTCTG CGATCAAGGT GGAAGCAGGG TTGGCTTCTT  
CTCAGGTGTC TGTCCTTGGC TGGTAGATGA CGCCGCTCCT CTTGGGTCT CACATGCTCT TTCTCTGTG TGTGCTGTC  
CCAATCTCTT CTTATAAGGA TGCAAGTCTT ATGGATCAGA GCACACCCCA ATGACCGTGT TTAACITGAA TCACCTCTTT  
AAAGTTTCTC TCTCAAATA CAATCACCTC CTGAGGCACT GTTAGGGCTT CGACACAGGA ATTCTTTTCC TAGGGGATTC  
55 AGTTCAGTCC AAAACGCCTA CCAGTGGAGA CTTGCAACAT GGGCGCCTGC TGGTCCCTCG CCAGGAATAT CACAGGCGAC  
TGTTCCTGT TGCATGGAAT AGAAGGCTAT TCCAGAGTAC TGTCTCTATT TATCAGATCT GGGATCTGG GAGAAGGGCA  
AAATAAAGTC CAAGTAGAAA AAAAAGCTAT GAAAGTTTGA GAGAGTAAAC ATAATTTCAG CCCGATGTGA AACGATCCTA  
GATTTACGCT GAAATAGTGA TGTGGGAAGT GAGGGGGGCC GGAATCAAGG CAGAGGGAAC AGCGTAACTG AAGGCATGGA  
AGGAGGGAAG TGTAGGCTGT GTTTGAAGAG TGGCAGCTGC TTCCACATT CTAACACACA GGATGTGATT TTGGGGTGTG  
60 TTGAGACAAG GCAGAAAACCT TGTTTGGAAA AATAACTTGA ATTCCCTGCA CATTTAAAAAT CTCTCAGCAG AAGAAAACCC  
CACTCAGAAC CCCACTGTTC ATTCTTGGC TTGATTTGG SCACAGCTGG CATAGCCCA GACTGAGTAA GCTCTTCA  
CACCTCATTT CATGAGTAGC CCCAAAGATC AATCATGGGC CAATTTCTTG GAAGAGAAGA CTCTCCGGTG TTTTGCAGTT  
ATTTGTTCTG CTTTCCGAG ATGTTCTCAA ATCGTTGAG CTACAAGCCA TGAGTCTGAA GTGTTTGTG TCCCTCCTTA  
CAGGTGGTAA CTTTCTACA GGCCTTGGCC ACAGATCTGA TCATTACAAT TGCGTCAGCA GTGGAGGGCA ATGTCTCTAT  
65 TCTGCCTGCC CGATCTTTAC CAAAATTCAA GGCACCTGTT ACAGAGGGA GGCACAGTGC TGCAAGTGAG CTGAGAGTGA  
CCAGAAGAAA TGACGAGAA GTGAAATGAA CTTTATAA GCATTTCTT AATAAAGGAA AATTGCTTTT GAAGTATACC  
TCTTTGGGC AAAATGAAT CTTGTGCTC AATTGGAAGA GGTAAAGAAG TAGGGGTTA GGGTGCATGG GTTGAACGT  
GAGACAGGTC GAACCACAAA GCCTGCCTGG AAAAGGGGAG TGACGCTCTA GGCTTCAGTG ATGTACCTC CACTTTGTTT  
GATCCACAAA CCAAGAGGTG ACTGATTTTG-3' (FRAG.NO: ) (SEQ ID NO:11843)  
70 5'-GCTCAGCCTC CAAGGAGCC AGCCTCTCCC CAGTCTCTGA AATCCTGAGT GTTGCTGCTC AGTCGCCATG AGAACTTCCT  
ACCTTCTGCT GTTTACTCTC TGCTTACTTT TGCTGAGAT GGCTCAGGT GGTAACTTTC TCACAGGCCCT TGGCCACAGA  
TCTGATCATT ACAATTCGCT CAGCAGTGA GGGCAATGTC TCTATTCTGC CTGCCGATC TTTACCAAAA TTCAAGGCAC  
CTGTTACAGA GGAAGGGCAA AGTGCTGCAA GTGAGCTGG AGTGACCAGA AGAAATGACG CAGAAGTGAA ATGAACCTTT  
TATAAGCATT CTTTAATAA AGGAAAATTG CTTTGAAGT AT-3' (FRAG.NO: ) (SEQ ID NO:11841)  
75 5'-CCGGGGG-3' (FRAG.NO:1800) (SEQ ID NO:1182)

5'-GG GCCTGCBGGG CC-3' (FRAG.NO:1801) (SEQ ID NO:11183)  
 5'-GGCBGCB BGG-3' (FRAG.NO:1802) (SEQ ID NO:11184)  
 5'-GGG TCC TCB TGG CTG GGG-3' (FRAG. NO:1212) (SEQ ID NO:10590)  
 5'-GCC TGG GCC TGC BGG GCC-3' (FRAG. NO:1213) (SEQ ID NO:10591)  
 5'-GCT CTT GCC TGG BGT GGC TC-3' (FRAG. NO:1214) (SEQ ID NO:10592)  
 5'-GCC CBG BGT CTT CCC TGG T-3' (FRAG. NO:1215) (SEQ ID NO:10593)  
 5'-CCGGGGCTGC BGCBBCTCB TCBGCTCTTG CCTGGGCTGG CTCBGCCTGG GCCTGCBGGG CCBCCBGGBG BBTGGCBGCB  
 BGGBTGGCB GGGTCCTCBT GGCTGGGGTC BCBGTCCTC TBGCTBGGCB GGGTGBCCBG BGBGGGC-3' (FRAG.NO:1803)  
 (SEQ ID NO:11185)

# **Human Defensin 2 Nucelic Acid and Antisense Oligonucleotide Fragments**

5'-ATCCTTTAAG TCAATGGACT TTGCATCAGT CACACCATCT TTTGTTACTT TGGACTTCCC CAGCTATGTT CAATAATTAC  
 TGTTCTTCCC TTGGGCCCA TTGTAATGGC TACAGCCTCG ACAAAAAAGTC TACACTTTGA AGCAITTAAGG CTCGGACATC  
 AGCACCAAAT TTTACATCTT TACCATCACT TCAAGTGAGG TGAGGAGCCA GTAGCCTGGA CACTGGTCTC ATCTGGTGAA  
 AGACTGTGGG TAATGGAAGC ATTCTGTGG GGTGCTGGCA GGACATGTGC ATGGCGAGGC AGGTCACTAG CAGCAAGTGA  
 15 GAGCTGCCCT TTACTTTCTA AAGGTGACAT AGCAAAATATA CAAAAAATAA TAAATAAATT ATTAATTAG GTAGAGCACA  
 TAAAGGCTTT ATTTCATATT CCATTCTCT GTATGTTTC TTCAACAGGA AGAAATAGTT TTAGTGTGAG GAATGAATGA  
 GTCTGCCCT CAATTCCAGC CTGCTCAACA CACAAGGAAA CAAAGCCCTG ACAATCAGAG TGAATCCCTG GTGACTAAGC  
 TCCAGTCTCT GGATGCATAT TTGTTTAGCA GTTCTGACAG CATTTGACCC AGCCCTCTCT CTGCATATCC CATCAGAACC  
 TTCTTTTCTT TTTTCTCTT TGAGACTGAG TCTTGCTCTG TCAGGAGCGA CTCCTGTGCC TCAGCCTCCC AAATACCTGG  
 20 AATTATAGGC GTAAAGCCATC ATGCCTGGCT AATTTTTGTA TTTTTCATGG AGATGGGGTT TTGCCATGTT GGTCAAATTG  
 GTCTCACACT CCTGACCTCA TGTGATCCAC CTGCTCAGC CTCCCAAACT GCTGGGATGA CAGGTGTAAG CCACCATGCT  
 AGGCTCAGAA ATTTCTTTT ATAAAAATGT CATTAAGGAT CTGGGCTGCA CAATATCGTT ACCAGCTTCC TTTAAATCCA  
 CTCTGGCTT GCCAGGAATC AGGTTCCTCA GAACCTGACA TTTTAAATGA AGAGGTGAGG CAGTTCATGA TTTAAAGCCTC  
 ATTGTCCCA TTGTCTGTG ACTGTGTCAC CCTGTGACAG TCACAGACAT GGACACTGGG GCCTGCTTGT TTCTCAAACT  
 25 GCCCTTAGAT CGAAAGAGGG AGGAACCAGG ATGAATGCCA CTCATTTTCC CAAGAAAGGC CCTCTCTGA GTGCCCCGGA  
 TGGGGCTCTG TCCATTGCC TGGGGCCGCA ATTGCTACT TGGGTTACGG AGGAAGGACA GGGTCTCTAG AGACACCAGA  
 GACCTCACAC AGCCCTGAAA ACATGGGGCT CCTTCCCAT TGTTTCCCAT CACCAACAGG GAGACCACTG GGAGGCTTGT  
 CAGCCCCACT CGGTGCTTCT CCACCAAAATC CCAAGGGCAG TGACGCTGAC GTCTGTGGAA AGCAGAGAAA GCCCTGGCTC  
 CCAAGCCCT GAAGTCCCTG TGGAGCTGAC ATTCCTCTGAG TGACGGTGTG AATGGAAGGA ACTCAAGTGC GGGTGGTAGG  
 30 CCACCTCTCT GCCCAGGCTT GGGTGAATC TGAGGGGACA CATGTAGTCA CAATCCCATC CTCCCATTTT CCTTCTCAGA  
 GGAAGGAAGT GGGCATCCAT CTGCCTCATC TCTCTCCGT GGGGAAGATG GGGAGTTTCA GGGGAACCTT CACATAAATT  
 TCACCAGCTC AGATCTCTG TGAGGATGGG GCCCACCATG CTCCCGGTGC TGCCAGAGGC CCTGAGCCCC TCCCAGGGCT  
 CCTGGGTTTG AGCCAGCCTG GTATCATCCC CAGGAGCTGA ATGTCAGAGC AATGGATAGA ATTAGATGGA AAGAGCTCTC  
 AATTGACCT GAGACTGTCC CCAGATACTC AGGAAAAACA GGACGTGCA CAGAGTGGGC CAGAGGTGAG AGCAGGTGTA  
 35 TAGGTCTCTG GTTTGAGTTT GTTCTCACGT GAGACAGACC CAGCCCTCA CTCCATTAC ACCTGGGTT TTAATAGGTG  
 CAAGATAGGA GCAATTTTCT GGTCCCAAGA GCAGGAGGAA GGGATTTTCT GGGGTTTCTT GAGTCCAGT TTGCATAAGA  
 TCTCTGAGT GTGCATTTT CTTTGAGGAC CATTTCTGA CTCACAGGT AAGTGGCTGA ATTTCAACCT CTGTAATGAG  
 CATTCACACC AATACAGTT CTGAATCTA CTGGGTGACC AGGGACCAGG ACCTTTATAA GGTGGAAGGC TTGATGTCT  
 CCCCAGACTC AGCTCCTGGT GAAGCTCCCA GCCATCAGCC ATGAGGGTCT TGTATCTCTT CTCTCTGTC CTCTCATAT  
 40 TCCTGATGCT TCTTCCAGT GAGATGGGCC AGGGAATAG GAGGGTTGGC CAAATGGAAG AATGGCGTAG AAGTTCTCTG  
 TCTCTCTCA TTCCCCTCA CCTATCTCTC CCTCATCCCT CTCTCTCTT CTCTCTCTG TGTGTCCCTT CCATCTCTTT  
 CTCTGCTTC TCTCTCTT TCCCTCTCTC TCTTTTCTT GTCTTTCTT TTCTCTCTT CCTAGAGCAT GTCTTTCTT  
 CTCTCTCTT CTTCTCTT ACCCACACTT TTAGACTGAA TGCCCTATTT AATTGAACAA AGCATTGCTT CTTCAATAG  
 AAAAGGAGTT TGAGAACCA ATGGACACCT CACTCGTCT TCTAAGCCAA TATGAAGGAG CCCAGTAGCT TGTAATATC  
 45 ATCTCTTCA TGTCTTCACT GCTACAACCT CTGAGACTAT GGTGAAACC TGTAGGTGA CTTTTTAAAT AAAAGGCAGA  
 AATTTTGATT TTATCTAAG AAAGTAGTAT AGAATGTGAT TTCTTAAAT TTATATTTA AAGGGTAGAT ACTGCAACCT  
 AGAGAATTCC AGATAATCTT AAGGCCAGC CTATACTGTG AGAACTACTG CAGCAAGACA CTCTGCCTCC AGGACTTTTC  
 TGATCAGAGG CCTGAGAAC AGTCCTGCC ACTAGGCCAC TGCAGGTCA CAGGACAGGG TACAGCCCAT TGAACCTCAT  
 TTTTAAACCT GGATGCTAAC CCTTCATTT CTCCTTGATA TTATGAAAAT AAAATAAAAA CCATGAAAGG ATAAAGAGG  
 50 GAGAGTGGAA GGAAGGATG GAGAAAGGGA AAAAGAAAAT TTGAGAGTAA ATCTTAAAC AATTAATCTA ATAGATATCA  
 TCTTGTGAAA TCTCATTTT ACCAATCTTA TTTATGAGT CTGGGTTTGT TGAGAACAAAT GGGGTTCTGA GAGGACCAGC  
 AGACCTCATG TTTTCAAAA CCTAGAACAG TATAATGAG GAAGCGGGG AGGCAGGGAG GCAGGAGGC AGGAGGCGAG  
 GGAGGCGGGC AGGTGGGAG GGAGGAGCGG AAGGAGGGAG GGAGGGAGGG AGGAGGGAGG GGAGGGAGTA AAAAAGAAGA  
 ATGAGGTTGA AACCAAGACT TAGATATTAG AAACAAGCCA TTACAAAAT TATTTCTATG GTTAATTGTG GTTTTCACT  
 55 GTAAGTTACT TGGTGTAAT TTCCTATTAA ACAATTTCAG TAAGTTGCAT CTTTTATCC CATCTCAGGT CAAATACTTA  
 ACAGACTAAA TGATTTGAAA AAGCAAAAGT TTAAGTGGCT GTGTGTGTTA AAATGGAGGT ATGGTGGCTT TGATATTATC  
 TTCTTGTGGT GGAGCTGAAT TCACAAGAGA TCGTTGCTGA GCTCTACCA GACCCACCT GGAGGCCCA GTCACTCAGG  
 AGAGATCAGG GTCTTTTCA ATCAGTTCTT ACAAATAA AACTCCCTCC AACCACAGCA GTGCCAGTT CCATGTTCAGA  
 AACTTAGATC CAAATGACTG ACTCGCTCT CATTATCATG ATGGAAAAGC CCAGGCTTGA GAAAGAAAGC CGCTGCGGAT  
 60 TTAATCAAGG CGATACTGAC ACAGGGTTTG TGTTTTCCA ACATGAGTTT TGAGTTCTTA CACGCTGTTT GCTCTTTTGT  
 TGTGTTTTT CCCTGTTAGG TGTTTTGGT GGTATAGGCG ATCTGTTAC CTGCCITAA AGTGGAGCCA TATGTCATCC  
 AGTCTTTTGC CTAGAAGGT ATAAACAAAT TGCCACCTGT GGTCTCCCTG GAACAAAATG CTGCAAAAAG CCATGAGGAG  
 GCCAAGAAGC TGCTGTGGCT GATGCGGATT CAGAAAGGGC TCCCTCATCA GAGACGTGCG ACATGTAAC CAAATTAAC  
 TATGGTGTC AAAGATACGC AATCTTTATC CTAGTAATTG TGGTCATTGG GTGATGTTGG TTTGGGCAGG CCATCTCTAA  
 65 TATCTTGAAA ACACCTTTT CTGCTTCCA GGAAGGGGTG AGGGCTGCCA CAGCGGGGCT TGGAGTGCTT TCCAGGGTCA  
 CAGGCATCTG TATTCTTGG ATCTCTGAC CTTCCTCAT TATTCCCGGC ATTTCTCTAA AACGTGTGCT TGTCTCTCC  
 TGCATCTCT CCTTGATGCT CCTCACCTT CCCATATCTT CCTTAAAAA AGCAAGGCCA ACTCAAAGC CAGTTCCTCT  
 ATGGAATCAT AGTGGATCTG CCAAGGGAGG GGATGCCAG TCCCTGTCTT TTCACAAAG TCCCTCTCTT TGGTAAAGG  
 70 TTCTTATGCA ATTAT GAATTCACAT TTCTCACCTT TTGATGATT AAGAAAGTAT GGAGAAATAT ATCTCTATC AATTTTTCAT  
 GCCTTCAATA ATTCTAAAT CATCAGTCAG TGTTTTCCA TCTTTTACTG TGATGATGCC CTTTCTTCCA AACTTTTTCA  
 TTGATCAGA GATGATGTTA CCAATTTCTT TGTCTCATG TGTGCAAAAT GTAGCAACCT TTGCAATTTT TCCAGGTTTG  
 GTCACAGGT TAGACTGCTT TTTAAGTTCA GCAATTACAG CATCAACAGC TAACATCACA CCTCTCTGA TTTCACTGG  
 ATTAGACCT TTGCTAACCT TCTGGAAGGC TTATTGGAA ATAGAGCATA CCAGTACAGC AGCAGTGAAG GTGCCATCCC  
 CCAGTCTCTC CATTTGTGT ATTGGCAACA TCTTGGCAA GTTAGCTCC AATGCTTTA TATTTATCTT TTAAGTCAAT  
 75 TGACTTTGCA TCAGTCACAC CATCTTTTGT TACTTTGGGA CTTCCTCAGC TATGTTCAAT AATTAAGTGT CTTCCTTTG

5 GCCCCATTGT AATGGCTACA GCATCGACAA AAAGTCTACA CTTTGAAGCA TTAAGGCTCA GACATCAGCA CCAAATTTTA  
CATCTTTACC ATCATTTCAA GTGAGGTGAG GAGCCAGTAG CCTGGACACT GGTCTCATCT GGTGAAAGAC TGTGGGTAAT  
GGAAGCATTT CTGTGGGGTG GTGGCAGGAC ATGTGATGAG TGAGGCAGGT CATCAGCAGC AAGTGAGAGC TGCCTCTTAC  
TTTCTAAAGG TGACATAGCA AGTATACAAA AAAAAATAAA ATATTAATTT AGGCAGAGCA CATAAAGGCT TTATTTCATA  
10 TTCCATTTCT CTGTATGCTT TCTTCACCAG GAAGAAATAG TTTTAGTGTC AGGAATGAAT GAGTCTGCCC CTCAATTCCA  
GCCTGCTCAG CACACAAGGA AACAAAGCCC TGACAATCAG AGTGACTCCC TGGTGAATAA GCTCCAGTCC TGGATGCATA  
TTTGTITAGC AGTTCTGACA GCATCTGACC GAGCCCTCTC TTTGCATACC CCACCAGAAC CTCTTTTTTT TTTTTTTTTC  
TTTGAGACTG AGTCTTGCTC TGTGCGAAGC GATTCCCGTG CCTCAGCCTC CCAAATACCT GGAATTATAG GCGTAAGCCA  
TCATGCTGG CTAATTTTTG TATTTTTCAT GGAGATGGGG TTTTGCCATG TTGGTCAAAT TGGTCTCACA CTCTGACCT  
15 CATGTGATCC ACCTGCCTCA GCCTCCCAAA GTGCTGGGAT GACAGGTGTA AGCCACCATG CTAGGCTCAG AAATTTCTTT  
TTATAAAAAA GTCATTAAGG ATCTTGCTG CACAATATCG TTACCAGCTT CCTTTAAATC CACCTCTGGC CTGCCAGGAA  
TCAGGGTCTC TCAGAACCTG ACATTTTAAA TGAAGAGGTC AGGCAGGTCA TGAGGAAAGC CTCATTGTCC CCATGTCTCT  
GTCAGTGTG ACACCCCTGAG ACATCACAGA CATGGACAT GGGGCTGCT TGTITCTCAA ACTGCCCTTA GATCGAAAGA  
GGGAGGAACC AGGATGAATG CCACCTATTT TCCCAAGAAA GGCCCTCTCC TGAGTGCCCG GGATGGGGCT CTGTCCATTG  
20 CCTGGGGCCC CCAATTGCTA CTCTGGGTTA CGGAAGAAGG ACAGGGTCTC GAGAGACACC AGAGACCTCA CACAGCCCTG  
AAAACATGGG GCTCCTTATC AAGTGTITCC CATCACCAAC AGGAGAGCCA CGTGGAGGCC TTGACGCCCT ACTCGGTGCT  
TCTGCCACAA ATCCAAAGGG CAGTGACGCT GACGTCTGTG AAAGCAGAG AAAGCCCTGG CTCCAAAGC CCTGATCTCC  
TGTGGAGCTG ACATTCCCTG AGTGACGGTG TGAATGGAAG GAACTCAAGT GCGGGTGGTA GGCCACCTCC TGGCCAGGC  
CTGGGTGAAC TCTGAGGGA CACATGTAGT CACAATCCCA TCCTCCCAT CTCTTCTCA GAGGAAGGAA GTGGGCATCC  
25 ATCTGCTCTA TCTCTCTCCC GTGGGGAAGA TGGGGAGTTT GAGGGAACT TTCACATAAA TTTCACCAGC CTGATCTCC  
TGTGAGGATG GGGCCACCA TGCTCCCGGT GCTGCCAGAG GCCCTGAGCC CCTCCAGGT CCCTGGGTTT GAGCCAGCCC  
TGTATCATCC CCAGGAGCTG AATGTCCGAA CAATGATAG AATTAGATGG AAAGAGCTCT CAATTTGGCC TGAGACTGTC  
CCCAGTACT CAGGAAAAAC AGGACGTGCG ACAGAGTGGG CAGCAGGTGA GTGGCAGGT ATAGTGCTTG ATAGTACTG  
TGTCTCAGC TGAGACAGAC CCAGCCCTC ACATCCATCA CACACTGGT TTTAAATGGT GCAAGATAG AGGAATTTTC  
30 TGGTCCCAAG AGCAGGAGGA AGGGATTTTC TGGGGTTTCC TGAGTCCAGA TTTGCATAAG ATCTCTGAG TGTGATGTT  
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 5'-GAATTCCTTG TAAGCCCTGT TACAGGGGCT GCACCCCA TACAACCTGA CCTGTGTCCA AGGCGGGCAA CTCAACCCCTT  
 AGATATTGAA TGGGTCCCAT GGCACCAATG CTTAAACACC AGCAGCCCTC ACAACCACAG ATCGTGTITT AAGGATGAGG  
 15 AGGTAGTTCT CTGGATGCAC AGGCTTCAAT CCAATAGGGC TCATGACGCC GCAGCACACA CCCAGTCTGC AGCCTGAAGA  
 GTTGGAGCAT TGCATTACA GAAAGCATCC AGACATGATC ATGGGCTCAG GGATACACCT GTTCTCCGAT GTGTACCACT  
 GAAGGATGGA AACTCTATG CTTCCACAGA AGCACCATC AAGCTTTTGC TGAATGCTTC TCTGAAGGCC CACAAGGCTG  
 AGAGGCTGTG CAACACCAGC AGTAAAGTGA ATGCCACGAC TCCACCTCC TTTCTGGGT GGCCATCTGG AAAGGCCACT  
 CCCACCTGA TGGTAATGC CTCAGACCAG TTTCTGGGCC AGATGATCCT AGACAATTGT TTAAGCTTAA ACTGTTCTAT  
 20 GGCCAAGCAA ACAGGTGATA GTACCTCTGG GGAACCACAT GCCGCTGTA CATCCAGATC TCAGGAGAAC CCAAAATGT  
 CTGTTCCACA TAGCAACAGA AGCCAGGTA GCACCTGATC TCACCTGGGT GTTCTCCAAC ATCCAGCTC AGCCAAATGG  
 CTTTCATTAG TTTTATGTT TAGACCCAG GTCTCGGGA CACTGCTTTA GAAACACATT CCAATCCTC CTCTGTGTGC  
 AGGTGGCAT CCAATCCAA TCTCTTGA GGGCGTATC TGTATACGC AGCCAGGCTG TCCAGAGGC CTAAATATT  
 CCCTTGGTGC AGGTAGTTCA GCTTAGCCAC CCAAGGTC TAACAGGTC AACTGTGTA GGAGCCATTG AGAATCCATA  
 25 GTTGGTGTCT GCCTGGGCT GGGCAGGGCT GACCAAGGTA GATGAGAGT TCCTCTGTGG AGTTCATCT TAACCTCACC  
 TTCCACCAA ATTCTCAAC TGTCTTGGC ACCACAATTA TTAATGGAC CCAACAGAAA GTAACCCCGG AAATAGGAC  
 ACCTCATCCC AAAAGACCTT TAAATAGGGG AAGTCCACTT GTGACGGCT GTCTCTGTCT ATAGAAGACC TGGACAGAG  
 GACTGTCTGC TGCCCTCTCT GGTCAACCTG CCTAGCTAGA GGATCTGTAA GTACTACAAA ACTTAAACTT TACACTGAGT  
 TTTTCATCT GAAGCTATGC CTCCAATCTG ACCTCTGACT GTGGGGCCGC CCCAGAGGGA CCCAGCGGGT GAATCCCTGC  
 30 TAGGAACGCT TGTCGGGACC TCTGGTACT CTGGGGGAC ATGGCTTCCA GCTAACTTAA TAGAGAAAT CAAGCAGTTT  
 CCTTCTAAAT ACACATGTCA CATGTCTGG TTAGCATGTC CAGTAAGAAG ACTATCACAG GTCTTGGAA CATCTTTTG  
 AGAGAAACCT ATTTAGGTCC TTGGTCTGTT TTTCAATCAG GTTGTGTTG TTTTGTCTAT GAGTGTGTGG AATTCTTAT  
 GTATTCAGAT ATTTGCCCT TCTGCCATGT AGGTTTIGCA AATATTTTCT CTCAITTTCT GGGTATCTT TTTCACTGGT  
 TGATTTGTTT CTGTCTGTG CAGATGCTT AGCGTTAAAT GAAGCCACAC TTGTCTATTT TCCCTTTTAT TGCTGTGCC  
 35 TTTGGTGTCA TAGCAAGAA ATCATTACCT ACATCAATGT CAAAAGCTTT ATCCTTCTAT ACACCTTCTAT TAGTTTATG  
 TTTCACTTGT TACATTTAGG TTTTCAATTC ATCTGAGTT GATGTCTTA CATGGTGTGA GATAAAGATT TAAATACATA  
 CATATATAAA ATCATGAGGT AGTGTACACT ATAAATATAC AATTGTAAAT TGTTACTCAA GTCTAAGTAG AGGTGGAAT  
 AATAACCTTT CTTTTITTTA CTTAAACCAC TCTGTGTCAT TGAGCTGATT TCACCTTTAG CCTGATAAAA TCATTGTCT  
 CTCCACCTG ATTCTACAG GAGACTACT ACCCATAGC CGAGTAAAC TCTTCATGAG GATGGTAAGT CACCTGAATC  
 40 CTGAAGTGAA TTAAGCTGTA TTCCATTGGA ACTCATATAG GACACCAGAA TCTAGACCTC CAGAGAACAG CAGGACCCAT  
 CTTCAGAAAA TAAGAAAGCAT TTGTTCCTG AGCCTGTGTA ATCAAGTGC AATTTCTATT CTTTGTGAA TGTAAAAAG  
 TGAATCAGAT TATTTAAGCA GGTGAACCCA CGAGTAACTC AGCAGGCTCT TCTTGTCTAT TATTAGCTCC AACCTAGCAC  
 AGACATTAAG GGTACAGATG TATACTAGCA TGAAGTGGG AGAACAGGAG CATTGAGCA ACCTTGAGAC CAATGGGCT  
 CTCTTATAAA ATGCACACCT CCTCTCACT AGATTGAGGA AGGTTTCTTG TCTCCGAGCC TTCTCCAGT AGAGCTATA  
 45 ATCCAGGCTG GCTCCTCCCT CCCACACAG CTGCTCCTG TCTCCCTCCT CCAGGTGACC CCAGCCATGA GGACCTCGC  
 CATCCTGTCT GCCATTCTCC TGGTGGCCCT GCAGGCCAG GCTGAGCCAC TCCAGGCAAG AGCTGATGAG GTTGTGTCAG  
 CCCCAGAGCA GATTGACGCG GACATCCAG AAGTGGTGT TCCCTTGTGA TGGGACGAAA GCTTGGCTCC AAAGACTCCA  
 CTATGACAG GAGTGCATGC AGAGCTGCTA AGTCTAGAGT GAAGGACGGG AGAGAGGTTT CAGAGTTGGT TCTCAGCAGT  
 50 CTATGCTACT GAGGTGGCTT CACTTAGAAT CTCTGGGCAT TGATTTTCTC ATCTAGAAAT TGAACAGAGA GCCAAATAAA  
 CCTGAGAAAC TTTATTTCTC CAAAGACTTG ATTTCCAAGAA ACATCTGTGA AATTCATAA GTTTAAGATA TGAAGAGACA  
 GACTAGTTAT TTCTGATCT AAACAAGTAG ACTTAGTTGT AAAGAGAACA TTTTACTCTA TCTACAGAAG AGCTTTTAAA  
 AACTGACGCC AAGCCTGAGG GTAAGTTTCA GTGTGTGTGT TAGGGGCGAG GAATGCAAAA ATGAGAGCAA AGGAGAAATGA  
 GTCTCAAAAT CTGTGTGACA AGCACTGCTC TGCGTGTITA TTCTATCGA CTGAGGTTGT TCGTGCTACC GGCTGCAATG  
 CAGCCAGCAT CACCTGTGAG CTAGCATGTG ACTTCCCGA GATCTTTTTT CTTACCCACT GCTAACTCCA TACTCAATTT  
 55 CTCTGTCTCT CCTGTGCCA GGCTCAAGGA AAAACATGGA CTGCTATTGC AGAATACCAG CGTGCAATTG AGGAGAACGT  
 CGCTATGGA CCGTGCATCTA CCAGGGAAGA CTCTGGGCAT TCTGTGCTG AGCTTGACA AAAAGAAAAA TGAGCTCAAA  
 ATTTGCTTTG AGAGCTACAG GGAATTGCTA TTAATCTGT ACCTTCTGCT CAATTTCTTT TCTCATCTC AAATAAATGC  
 CTGTGTACAA GATTTCTGTG TTTCCACCTC TTTAATGTG GATATGTGTC TGTGTCAAGA CACTTGGGAT ACACGTACCA  
 AAACGCAAAA TCAATTTTTT GAACAATATA-3' (FRAG. NO: ) (SEQ ID NO:11846)  
 5'-GGCBGCBGGG-3' (FRAG. NO:1805) (SEQ ID NO:11187)  
 5'-GG CTG GGG-3' (FRAG. NO:1806) (SEQ ID NO:11188)  
 5'-GGGGTCCBCC-3' (FRAG. NO:1807) (SEQ ID NO:11189)  
 5'-GGG TCC TCB TGG CTG GGG TC-3' (FRAG. NO:1216) (SEQ ID NO:10594)  
 5'-CCT CTC TCC CGT CCT-3' (FRAG. NO:1217) (SEQ ID NO:10595)  
 65 5'-CGCTGCBBTC TGCTCCGGGG CTGCBGCBBC CTCBTBGGCTC TTGCCTGGBGTG GCTCBGCCTGG GCCTGCBGGG  
 CCBCCBGGGB BTGGCBGGBG BGTGGCBGGG TCCTBTGGC TGGGTCBCTT GGBGBGGGB GBGCBGG-3' (FRAG.  
 NO:1808) (SEQ ID NO:11190)

#### Human Macrophage Inflammatory Protein-1-alpha/RANTES

#### Receptor Nucleic Acid and Antisense Oligonucleotide Fragments

- 70 5'-GTCTTTGTTT CTGGGCTCGT GCCCCBTCCC GGCTTCTCTC TGGTCCGTC CTCTGTGGTG TTTGGCCCTG CTTCCTTTTG  
 CCTGTGAGG GGGCAGCAGT TGGGCCCAA AGGCCCTCTC GTTCACCTTC TGGCACGAGTT GCATCCCCATA GTCAAACTCT  
 GTGGTCTGT CATAGTCTCT TGTGGTGTG GGAGTTTCCA TCCCGGCTTC TCTCTGGTTC CAAGGGAGB GGGGGCBGB  
 GTTGGGCCCC BBBGGCCCTC TCGTTCBCT TCTGGCBGCG BGTTGCBTCC CCBTBTBCTB BCTCTGTGGT CGTGTCTBGB  
 TCCTCTGTGG TGTTTGGBGT TTCCBTCCCG GCTTCTCTCT GTTCCBGG GB-3' (FRAG. NO:1809) (SEQ ID NO:11191)



- 5'-GGGCC CC-3' (FRAG. NO:1810) (SEQ ID NO:11192)  
 5'-GGGGGCBGC-3' (FRAG. NO:1811) (SEQ ID NO:11193)  
 5'-CCCGGCTTC-3' (FRAG. NO:1812) (SEQ ID NO:11194)  
 5'-GTC TTT GTT TCT GGG CTC GTG CC-3' (FRAG. NO:1218) (SEQ ID NO:10596)  
 5'-CCB TCC CGG CTT CTC TCT GGT TCC-3' (FRAG. NO:1219) (SEQ ID NO:10597)  
 5'-GTC CTCTGT GGT GTT TGG-3' (FRAG. NO:1220) (SEQ ID NO:10598)  
 5'-CCC TGC TTC CTT TTG CCT GTT-3' (FRAG. NO:1221) (SEQ ID NO:10599)  
 5'-GAGGGGGCAG CAGTTGGGCC CCAAAGGCC TCTCGTTCAC CTCTGGCAC GGAGTTGCAT CCCCATAGTC AAACCTCTGTG  
 10 5'-GTCATAGTCTCTGTGGTGTGGAGTTTCCATCCCGGCTTCTCTGTGGTTCCAAGGGA-3' (FRAG. NO:1223) (SEQ ID NO:10601)  
 5'-GBGGGGGCBG CBGTTGGGCC CBBBGGGCC TCTCGTTCBC CTCTGGCBC GGBGTTGCBT CCCCBTGTGCT BBBCTCTGTG  
 5'-TCBTGTCTCTGTGGTGTGGGTTCBTTCCBCCCGGCTTCTCTGTGGTTCCBGGGB-3' (FRAG. NO:1225) (SEQ ID NO:10603)  
 RANTES Antisense Oligonucleotide Fragments  
 15 5'-GGGCBGCGGG CBGTGGGCGG GCBTGTBGG CBBBGBGCB GGGTGTGGTG TCCGBGGBBT BTGGGGBGGC BGBTGCBBG  
 GCGCBGBGGG CBGTBGCBBT GBGGBTGBCB GCGBGGCGTG CCGCGGBGBC CTTCBTGGTB CCTGTGGBGB GGCTGTGCGB  
 GGGGTGTGGT GTCCGCTTG GCGGTCTTT CCGGTGTTTCTCTCTGGT TGGCCTGCTG CTCGTCGTGT CGCTCCGCTC  
 CCGGGTTCGT CTCGCTCTGT CGCCCCCTCC TTCTGTGTCG TGTTCTCTCC TTCCTTGCTCT CT-3' (FRAG. NO: 1813) (SEQ ID  
 NO:11195)  
 20 5'-GGGTTGGC-3' (FRAG. NO: 1814) (SEQ ID NO:11196)  
 5'-CGGGG CBG-3' (FRAG. NO: 1815) (SEQ ID NO:11197)  
 5'-CCCGGGTTCG-3' (FRAG. NO: 1816) (SEQ ID NO:11198)  
 5'-GGGTGTGCTG-3' (FRAG. NO: 1817) (SEQ ID NO:11199)  
 5'-GGGCBGCGGG CBGTGGGCGG GCBTGTBGG CBBBGBGCB GGGTGTGGTG TCCGBGGBBT BTGGGGBGGC BGBTGCBBG  
 25 GCGC-3' (FRAG. NO:1226) (SEQ ID NO:10604)  
 5'-BGBGGGCBGTB GCBTGBGGB TGBCBGCGBG GCGTGCCGCG GBGBCCTTCB TGGTBCCTGT GGBGBGGCTG TCGGBGG-3'  
 (FRAG. NO:1227) (SEQ ID NO:10605)  
 5'-GGGTGTGTGTCGCTTGGCGGTCTTTCGGGTGTTCTCTCTGGTGTGGCTGCTGCTCGTCTGCTG-3' (FRAG. NO:1228) (SEQ  
 ID NO:10606)  
 30 5'-GCTCCGCTCCCGGTTCTGCTCTGCTCGCCCCCTTCTCTGCTGTGCTCTCCCTTCTTGCCTCT-3' (FRAG. NO:1229)  
 (SEQ ID NO:10607)  
 5'-GGGTGTGGTGTCCG-3' (FRAG. NO:1230) (SEQ ID NO:10608)  
 5'-CTTGGCGGTTCTTTTCGGGTG-3' (FRAG. NO:1231) (SEQ ID NO:10609)  
 5'-TTCTTCTCTGGGTGGC-3' (FRAG. NO:1232) (SEQ ID NO:10610)  
 35 5'-CTGCTGCTGCTGCTGCTG-3' (FRAG. NO:1233) (SEQ ID NO:10611)  
 5'-GCTCCGCTCCCGGGTTC-3' (FRAG. NO:1234) (SEQ ID NO:10612)  
 5'-GTCTGCTCTGTCGCCC-3' (FRAG. NO:1235) (SEQ ID NO:10613)  
 5'-CTTCTCTCTGTC-3' (FRAG. NO:1236) (SEQ ID NO:10614)  
 5'-GTGTTCCTCCCTTCTTGCCTCT-3' (FRAG. NO:1237) (SEQ ID NO:10615)  
 40 5'-GGGCBGCGGG CBGTGGGCGG GCBTGTBGG CBBBGBGCB GGGTGTGGTG TCCGBGGBBT BTGGGGBGGC BGBTGCBBG  
 GCGCBGBGGG CBGTBGCBBT GBGGBTGBCB GCGBGGCGTG CCGCGGBGBC CTTCBTGGTB CCTGTGGBGB GGCTGTGCGB GG-3'  
 (FRAG. NO:1818) (SEQ ID NO:11200)  
**Human Muscarinic Acetylcholine Receptor HM1 Nucleic Acid and Antisense Oligonucleotide Fragments**  
 5'-GCTGCCGGC GGGGTGTGCG CTTGGCGCTC CCGTGCTCGG TTCTGTCT CCGGTCCCC CTTCCTGCG GTCTCGGGCC  
 45 TTCGCTCTT TCCTTCTTT CTTCCGCTC CGTGGGGGCT GCTTGGTGG GGCCTGTGCT CCGGGTCCCG GGGCTTCTGG  
 CCCTGCGCT TCATGGTGG TAGGTGGGG GTTCBTGGTG GCTBGGTGG GC-3' (FRAG. NO:1819) (SEQ ID NO:11201)  
 5'-GGTGGGGC-3' (FRAG. NO:1820) (SEQ ID NO:11202)  
 5'-GCCCGGCGGG-3' (FRAG. NO:1821) (SEQ ID NO:11203)  
 5'-CGG GGC TTC TGG CCC-3' (FRAG. NO:1822) (SEQ ID NO:11204)  
 50 5'-GTT CBT GGT GGC TBG GTG GGG C-3' (FRAG. NO:1238) (SEQ ID NO:10616)  
 5'-GCT GCC CGG CGG GGT GTG CGC TTG GC-3' (FRAG. NO:1239) (SEQ ID NO:10617)  
 5'-GCT CCC GTG CTC GGT TCT CTG TCT CCC GGT-3' (FRAG. NO:1240) (SEQ ID NO:10618)  
 5'-CCC CCT TTG CCT GGC GTC TCG G-3' (FRAG. NO:1241) (SEQ ID NO:10619)  
 5'-GCC TTC GTC CTC TTC CTC CTT CC-3' (FRAG. NO:1242) (SEQ ID NO:10620)  
 55 5'-GCT CCG TGG GGG CTG CTT GGT GGG GGC CTG TGC CTC GGG GTC C-3' (FRAG. NO:1243) (SEQ ID NO:10621)  
 5'-CGG GGC TTC TGG CCC TTG CC-3' (FRAG. NO:1244) (SEQ ID NO:10622)  
 5'-GTT CAT GGT GGC TAG GTG GGG C-3' (FRAG. NO: 1245) (SEQ ID NO:10623)  
**Human Muscarinic Acetylcholine Receptor HM3 Nucleic Acid and Antisense Oligonucleotide Fragments**  
 5'-GGG GTG GGT BGG CCG TGT CTG GGGTT GGC CBT GTT GGT TGC CTCT TGG TGG TGC GCC GGG CGCG TCT TGG CTT TCT  
 60 TCT CCT TCG GGC CCT CGG GCC GGT GCT TGT GGGCT CCT CCC GGG CGG CCT CCC CGG GCG GGG GCT TCT TGGCG CTG  
 GCG GGG GGG CCT CCGTCT CTG TGG CTG GGC GTT CCT TGG TGT TCT GGG TGGTGG CGG GCG TGG TGG CCT CTG TGGGG  
 CCC GCG GCT GCB GGG GTTG CCT GTC TGC TTC GTCTT TGC GCT CCC GGG CCG CCGGG GTG GGT AGG CCG TGT CTG  
 GGGGT GGC CAT GTT GGT TGC CGGG CCC GCG GCT GCA GGG G-3' (FRAG. NO:1823) (SEQ ID NO:11205)  
 5'-CCC GGG CGG-3' (FRAG. NO:1824) (SEQ ID NO:11206)  
 65 5'-G GCG GGG GGG CC-3' (FRAG. NO:1825) (SEQ ID NO:11207)  
 5'-CCC GGG CCG CC-3' (FRAG. NO: 1826) (SEQ ID NO:11208)  
 5'-GG CCG TGT-3' (FRAG. NO:1827) (SEQ ID NO:11209)  
 5'-GGG GTG GGT BGG CCG TGT CTG GGG-3' (FRAG. NO:1246) (SEQ ID NO:10624)  
 5'-GTT GGC CBT GTT GGT TGC C-3' (FRAG. NO:1247) (SEQ ID NO:10625)  
 70 5'-TCT TGG TGG TGC GCC GGG C-3' (FRAG. NO:1248) (SEQ ID NO:10626)  
 5'-GCG TCT TGG CTT TCT TCT CCG GGC CCT CGG GCC GGT GCT TGT GG-3' (FRAG. NO:1249) (SEQ ID NO:10627)  
 5'-GCT CCT CCC GGG CGG CCT CCC CGG GCG GGG GCT TCT TG-3' (FRAG. NO:1250) (SEQ ID NO:10628)  
 5'-GCG CTG GCG GGG GGG CCT CCT CC-3' (FRAG. NO:1251) (SEQ ID NO:10629)  
 5'-GCT CTG TGG CTG GGC GTT CCT TGG TGT TCT GGG TGG C-3' (FRAG. NO:1252) (SEQ ID NO:10630)

- 5'-TGG CGG GCG TGG TGG CCT CTG TGG TGG-3' (FRAG. NO:1253) (SEQ ID NO:10631)  
 5'-GGG CCC GCG GCT GCB GGG G-3' (FRAG. NO:1254) (SEQ ID NO:10632)  
 5'-TTG CCT GTC TGC TTC GTC-3' (FRAG. NO:1255) (SEQ ID NO:10633)  
 5'-CTT TGC GCT CCC GGG CCG CC-3' (FRAG. NO:1256) (SEQ ID NO:10634)  
 5'-GGG GTG GGT AGG CCG TGT CTG GGG-3' (FRAG. NO:1257) (SEQ ID NO:10635)  
 5'-GTT GGC CAT GTT GGT TGC C-3' (FRAG. NO:1258) (SEQ ID NO:10636)  
 5'-GGG CCC GCG GCT GCA GGG G-3' (FRAG. NO:1259) (SEQ ID NO:10637)
- Human Fibronectin Antisense Oligonucleotide Fragments**
- 5'-CGG TTT CCT TTG CCG TC TTG GCC CGG GCT CCG GGT G CCC GCC CGC CCG CCG GCC GCC GC CCC GCC GGG CTG TCC  
 CCG CCC CGC CCC GGC CCG GGG CGC GGG GG CGG CCC TCC CGC CCC TCT GG GCC GGC GCG GGC GTC GG CCG CTC GCG  
 CCT GGG GTT CCC TCT CCT CCC CCT GTG C GCC TGC CTC TTG CTC TTCTGC GTC CGC TGC CTT CTC CC CTC TCC TCG GCC  
 GTT GCC TGT GCC TGT CCG TCC TGT CGC CCT TCC GTG GTG C TGT TGT CTC TTC TGC CCT C GGT GTG CTG GTG CTG GTG  
 GTG GTG CCT CTG CCC GTG CTC GCCCTG CCT GGG CTG GCC TCT TCG GGT GTG GCT TTG GGG CTC TCT TGG TTG CCC TTT  
 CTT CTC GTG GTG CCT CTC CTC CCT GGC TTG GTC GT TGT CTG GGG TGG TGC TCC TCT CCC TTT CCC TGC TGG CCG TTT GT  
 CCT GTT TTC TGT TGT CCT CT TTC CTC CTG TTT CTC CGT TTG GCT TGC TGC TTG CCG GGC TGT CTC C TTT GCC CCT GTG  
 GGC TTT CCC TGG TCC GGT CTT CTC CTT GGG GGT C GCC CTT CTT GGT GGG CTGGCT CGT CTG TCT TTT TCC TTC C TGG  
 GGG TGG CCG TTG TGG GCG GTG TGG TCC GCC T TGC CTC TGC TGG TCT TTC-3' (FRAG. NO:1828) (SEQ ID NO:11210)  
 5'-GGCCCGGGC-3' (FRAG. NO:1829) (SEQ ID NO:11211)  
 5'-GCCGGCGCGGGCG-3' (FRAG. NO:1830) (SEQ ID NO:11212)  
 5'-GCCTGGGCTGGCC-3' (FRAG. NO:1831) (SEQ ID NO:11213)  
 5'-GGGGG TGCCG-3' (FRAG. NO:1832) (SEQ ID NO:11214)  
 5'-GG GGG TGG CCG TTG TGG GCG G-3' (FRAG. NO:1833) (SEQ ID NO:11215)  
 5'-CGG TTT CCT TTG CCG TC-3' (FRAG. NO:1260) (SEQ ID NO:10638)  
 5'-TTG GCC CCG GCT CCG GGT G-3' (FRAG. NO:1261) (SEQ ID NO:10639)  
 5'-CCC GCC CGC CCG CCG GCC GCC GC-3' (FRAG. NO:1262) (SEQ ID NO:10640)  
 5'-CCC GCC GGG CTG TCC CCG CCC CGC CCC-3' (FRAG. NO:1263) (SEQ ID NO:10641)  
 5'-GGC CCG GGG CGC GGG GG-3' (FRAG. NO:1264) (SEQ ID NO:10642)  
 5'-CGG CCC TCC CGC CCC TCT GG-3' (FRAG. NO:1265) (SEQ ID NO:10643)  
 5'-GCC GGC GCG GGC GTC GG-3' (FRAG. NO:1266) (SEQ ID NO:10644)  
 5'-CCG CTC GCG CCT GGG GTT CCC TCT CCT CCC CCT GTG C-3' (FRAG. NO:1267) (SEQ ID NO:10645)  
 5'-GCC TGC CTC TTG CTC TTC-3' (FRAG. NO:1268) (SEQ ID NO:10646)  
 5'-TGC GTC CGC TGC CTT CTC CC-3' (FRAG. NO:1269) (SEQ ID NO:10647)  
 5'-CTC TCC TCG GCC GTT GCC TGT GC-3' (FRAG. NO:1270) (SEQ ID NO:10648)  
 5'-TGT CCG TCC TGT CGC CCT TCC GTG GTG C-3' (FRAG. NO:1271) (SEQ ID NO:10649)  
 5'-TGT TGT CTC TTC TGC CCT C-3' (FRAG. NO:1272) (SEQ ID NO:10650)  
 5'-GGT GTG CTG GTG CTG GTG GTG GTG-3' (FRAG. NO:1273) (SEQ ID NO:10651)  
 5'-CCT CTG CCC GTG CTC GCC-3' (FRAG. NO:1274) (SEQ ID NO:10652)  
 5'-CTG CCT GGG CTG GCC TCT TCG GGT-3' (FRAG. NO:1275) (SEQ ID NO:10653)  
 5'-GTG GCT TTG GGG CTC TCT TGG TTG CCC TTT-3' (FRAG. NO:1276) (SEQ ID NO:10654)  
 5'-CTT CTC GTG GTG CCT CTC CTC CCT GGC TTG GTC GT-3' (FRAG. NO:1277) (SEQ ID NO:10655)  
 5'-TGT CTG GGG TGG TGC TCC TCT CCC-3' (FRAG. NO:1278) (SEQ ID NO:10656)  
 5'-TTT CCC TGC TGG CCG TTT GT-3' (FRAG. NO:1279) (SEQ ID NO:10657)  
 5'-CCT GTT TTC TGT TGT CTT CCT CT-3' (FRAG. NO:1280) (SEQ ID NO:10658)  
 5'-TTC CTC CTG TTT CTC CGT-3' (FRAG. NO:1281) (SEQ ID NO:10659)  
 5'-TTG GCT TGC TGC TTG CCG GGC TGT CTC C-3' (FRAG. NO:1282) (SEQ ID NO:10660)  
 5'-CTT GCC CCG GTG GGC TTT CCC-3' (FRAG. NO:1283) (SEQ ID NO:10661)  
 5'-TGG TCC GGT CTT CTC CTT GGG GGT C-3' (FRAG. NO:1284) (SEQ ID NO:10662)  
 5'-GCC CTT CTT GGT GGG CTG-3' (FRAG. NO:1285) (SEQ ID NO:10663)  
 5'-GCT CGT TCT TTT TCC TTC C-3' (FRAG. NO:1286) (SEQ ID NO:10664)  
 5'-TGG GGG TGG CCG TTG TGG GCG GTG TGG TCC GCC T-3' (FRAG. NO:1287) (SEQ ID NO:10665)  
 5'-TGC CTC TGC TGG TCT TTC-3' (FRAG. NO:1288) (SEQ ID NO:10666)
- Human Interleukin-1 (IL-1) Nucleic Acid and antisense Oligonucleotide Fragments**
- 5'-AAGCTTCTAC CCTAGTCTGG TGCTACACT ACATTGCTTA CATCCAAGTG TGGTATTTCT TGTGGCTCCT GTTATACTA  
 TTATAGCACC AGGTCTATGA CCAGGAGAAT TAGACTGGCA TTAAATCAGA ATAAGAGATT TTGCACCTGC AATAGACCTT  
 ATGACACCTA ACCAACCCCA TTATTACAA TTAAACAGGA ACAGAGGGAA TACTTTATCC AACTCACACA AGCTGTTTTC  
 CTCCAGATC CATGCTTTT TGCGTTTATT ATTTTITAGA GATGGGGGCT TCACTATGTT GCCACACTG GACTAAAACT  
 CTGGGCCCTCA AGTGATTGTC CTGCCCTCAGC CTCCTGAATA GCTGGGACTA CAGGGGCATG CCATCACACC TAGTTTCATTT  
 CCTCTATTGA AAATATACAT GGCCTAAACT CCAACTGGGA ACCCAAAACA TTCAITTTGCT AAGAGTCTGG TGTTCTACCA  
 CCTGAACCTAG GCTGGCCACA GGAATTATAA AAGCTGAGAA ATTCTTTAAT AATAGTAACC AGGCAACATC ATTGAAGGCT  
 CATATGTAAA AATCCATGCC TTCTTTCTC CCAATCTCCA TTCCCAAACT TAGCCACTGG TTCTGGCTGA GGCCTTACGC  
 ATACCTCCCG GGGCTTGAC ACACCTTCTT CTACAGAAAG CACACCTTGG GCATATCCTA CAGAAGACCA GGCTTCTCTC  
 TGGTCTTGG TAGAGGGCTA CTTTACTGTA ACAGGGCCAG GGTGGAGAGT TCTCTCTGA AGCTCCATCC CTTCTATAGG  
 AAATGTGTTG ACAATATCA GAAGAGTAAG AGGATCAAGA CTCTTTGTG CTCAAATACC ACTGTCTCT TCTTACCCT  
 GCCCTAACCA GGAGCTTGTC ACCCCAACT CTGAGGTGAT TTATGCCTTA ATCAAGCAAA CTTCCTCTT CAGAAAAGAT  
 GGCTCATTTT CCCTCAAAAG TTGCCAGGAG CTGCCAAGTA TTCTGCCAAT TCACCCTGGA GCACAATCAA CAAATTCAGC  
 CAGAACACAA CTACAGCTAC TATTAGAACT ATTATTATTA ATAAATTCCT CTCCAAATCT AGCCCTTGA CTTCCGATTT  
 CACGATTTCT CCCTTCTCC TAGAACTTG ATAAGTTTCC CGGCTTCCC TTTTCTAAG ACTACATGTT TGTCATCTTA  
 TAAAGCAAAG GGGTGAATAA ATGAACCAAA TCAATAACTT CTGGAATATC TGCAAAACA ATAAATATCA GCTATGCCAT  
 CTTTCACTAT TTTAGCCAGT ATCGAGTTGA ATGAACATAG AAAAATACAA AACTGAATTC TTCCCTGTAA ATTCCCGTT  
 TTGACGACGC ACTTGATGCC ACGTAGCCAC GCCTACTTAA GACAATTACA AAAGGCGAAG AAGACTGACT CAGGCTTAAG  
 CTGCCAGCCA GAGAGGGAGT CATTTCAATT GCGTTTGAGT CAGCAAAGGT ATTGTCTCA CATCTCTGCC TATTAAGTA  
 TTTTCTGTTG TTGTTTTCCT TTTCTCTCAG ATTGCTTCT CTAAAGCTAC AGTCTCTCCT TTCTTTCTT  
 GTCCCTCCCT GGTGTGTAT GTGACCTAGA ATTACAGTCA GATTTCAGAA AATGATTCTC TCATTTTGT GATAAGGACT  
 GATTGTTTT ACTGAGGGAC GGCAGAACTA GTTTCCTATG AGGCGATGG TGAATACAAC TGAGGCTTCT CATGGGAGGG

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75 AAAAATCAA TTGTATGTGA CTGCCCAAGA TGAAGACCAA CCAAGTGTGCT TGAAGGAGAT GCCTGAGATA CCAAAACCA

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(FRAG. NO: 1)(SEQ ID NO: 11884)

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**Human Interleukin-1 Receptor (IL-1 R) Nucleic Acids and Anti-sense Oligonucleotide Fragments**

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 25 CACTAGGAGT ATTGAGCTAC GCATCAAGAA AAAAAAGAA GAGACCATTC CTGTGATCAT TTCCCCCTC AAGACCATAT  
 CAGCTTCTCT GGGGTCAAG CTGACAATCC GTGTAAAGGT GTTTCTGGGA ACCGGCACAC CCTTAACCCAC CATGCTGTG  
 TGGACGGCCA ATGACACCCA CATAGAGAGC GCCTACCCGG GAGGCCGCGT GACCGAGGGG CCACGCCAGG AATATTAGA  
 AAATAATGAG AACTACATTG AAGTGCCATT GATTTTGTAT CCTGTACAA GAGAGGATTT GCACATGGAT TTAAATGTG  
 TTGTCCATA TACCCTGAGT TTTCAGACAC TACGCACCAC AGTCAAGGAA GCCTCTCTCA CGTCTCTCTG GGCATTGTG  
 CTGGCCCCAC TTTCATGGC CTTCTTGGTT TTGGGGGGA TATGGATGCA CAGACGGTGC AAACACAGAA CTGGAAGAGC  
 30 AGATGGTCTG ACTGTGCTAT GGCTCATCA TCAAGACTTT CAATCCTATC CCAAGTGAAG TAAATGGAAT GAAATAATTC  
 AAACACAAAA AAAAAA-3' (FRAG. NO.:)(SEQ ID NO:11887)  
 5'-GCCGGAGCCG ACTCGGAGCG CGCGGCGCGC CGGGCGCGGC CGGGCGCGGC GTGGGGGCGC CGGCTGCCCC  
 GCGCGCCCAG GGAGCGGCAG GAATGTGACA ATCGCGCGCC CGCACCGTAG CACTCCTCGC TCGGCTCCTA GGGCTCTGCG  
 CCTCTGAGCT GAGCCGGGTT CCGCCCGGGC TGGGATCCCA TCACCTCCA CGGCCGTCG TCCAGGTAGA CGCACCTCT  
 35 GAAGATGGTG ACTCCCTCT GAGAAGCTGG ACCCTTGGT AAAAGACAAG GCCTTCTCCA AGAAGATATA GAAAGTGTTA  
 CTCAGACTTA TTGTTTCTAT AGCTCTACTG ATTTCTTCTC TGGAGGCTGA TAAATGCAAG GAACGTGAAG AAAAAATAAT  
 TTAGTGTCA TCTGCAATG AAATTGATGT TCGTCCCTGT CCTCTTAAC CAAATGAACA CAAAGGCACT ATAACITGGT  
 ATAAAGATGA CAGCAAGACA CCTGTATCTA CAGAACAAGC CTCCAGGATT CATCAACACA AAGAGAAACT TTGGTTTGT  
 40 CTTGCTAAGG TGAAGGATTC AGGACATTAC TAATGCGTGG TAAGAAATTC ATCTTACTGC CTCAGAATTA AAATAAGTGC  
 AAAATTTGTG GAGAATGAGC CTAACCTATG TTATAATGCA CAAGCCATAT TTAAGCAGAA ACTACCCGTT GCAGGAGACG  
 GAGGACTTGT GTGCCCTTAT ATGGAGTTT TAAAAATGA AAATAATGAG TTACCTAAAT TACAGTGGTA TAAGGATTGC  
 AAACCTCTAC TTCTTGACAA TATACACTTT AGTGGAGTCA AAGATAGGCT CATCGTGATG AATGTGGCTG AAAAGCATAG  
 AGGGAACAT ATCTGTCAATG CATCCTACAC ATACTTGGGC AAGCAATATC CTATTACCCG GGTAATAGAA TTTATTACTC  
 TAGAGGAAAA CAAACCCACA AGGCCTGTGA TTGTGAGCCC AGCTAATGAG ACAATGGAAG TAGACTTGGG ATCCAGATA  
 45 CAATTGATCT GTAATGTAC CGGCCAGTTG AGTGACATTG CTTACTGGAA GTGGAATGGG TCAGTAATTG ATGAAGATGA  
 CCAAGTGCTA GGGGAAGACT ATTACAGTGT GGAATAACCT GCAACAAAA GAAGGAGTAC CCTCATACA GTGCTTAATA  
 TATCGGAAAT TGAAGTAGA TTTTATAAAC ATCCATTAC CTGTTTTGCC AAGAATACAC ATGGTATAGA TGCAGCATAT  
 ATCCAGTTAA TATATCCAGT CACTAATTTT CAGAAGCACA TGAATGGTAT ATGTGTACG TTGACAGTCA TAATTGTGTG  
 50 TTCTGTTTTT ATCTATAAAA TCTTCAAGAT TGACATTGTG CTTTGGTACA GGGATTCTG CTATGATTTT CTCCCAATA  
 AAGCTTACA TGGAAGACC TATGACGCAT ATACATTGTA TCCAAAGACT GTTGGGGAAG GTTGTACCTC TGACTGTGAT  
 ATTTTGTGT TTAAGTCTT GCCTGAGGTC TTGAAAAAC AGTGTGGATA TAAGCTGTTT ATTTATGGA GGGATGACTA  
 CGTTGGGGAA GACATTGTG AGGTCAATTA TGAACACGTA AAGAAAAGCA GAAGACTGAT TATCATTTTA GTCAGAGAAA  
 CATCAGGCTT CAGCTGGCTG GGTGGTTCAT TGAAGAGCA AATAGCCATG TATAATGCTC TTGTTACAGA TGAATTAATA  
 55 GTTGTCTGCTG TTGAGCTGGA GAAAATCCAA GACTATGAGA AATGCCAGA ATCGATTAAA TTCATTAAGC AGAAACATGG  
 GGCTATCCGC TGGTCAGGGG ACTTTACACA GGGACCACAG TCTGCAAGA CAAGGTTCTG GAAGAATGTC AGGTACCACA  
 TGCCAGTCCA GCGACGGTCA CTTTATCTA AACACCAGT ACTGTACCA GCCACTAAGG AGAACTGCA AAGAGAGGCT  
 CACGTGCCTC TCGGGTAGCA TGGAGAAGTT GCCAAGAGTT CTTAGGTGTC CTCCTGTCTT ATGGCGTTG AGGCCAGGTT  
 ATGCCTCATG CTGACTTGCA GAGTTCATGG AATGTAATA TATCATCCTT TATCCCTGAG GTCACCAGGA ATCAGG-3' (FRAG.  
 NO.:)(SEQ ID NO:11888)  
 60 **Human Interleukin-8 Fragments Antisense Oligonucleotide Fragments**  
 5'-GBTGTGTTGTT BCCBBBGBT CBBGBBGBG TTTGCTBTCT BBGBBGBT BTTBGBBGBT GGBBBBGBG GTBGGTGBGBB  
 BGBTGTGCTT BCCTTCBGB BGGGTGCBG BBBTCBGBBGG CTGCCBGBGBG CCBGCGCCBGC TTGGBTGCT GTTTBGBGB  
 BGTGBGGTGC TCCGGTGGCT TTTGCTGTG GTGCTCTGCT GTCTCTG TTC CTTCGGGTGG TTTCTTCTG GCTCTGTGC  
 TTTCTTGTG CCCTTGGCCC-3' (FRAG. NO:1834) (SEQ ID NO:11216)  
 65 5'-G CTC CGG-3' (FRAG. NO:1835) (SEQ ID NO:11217)  
 5'-CBBGBBGBG-3' (FRAG. NO:1836) (SEQ ID NO:11218)  
 5'-CBGBB BGTGBGGTGC-3' (FRAG. NO:1837) (SEQ ID NO:11219)  
 5'-BCCBBBGBB CBBGBBGBG-3' (FRAG. NO:1838) (SEQ ID NO:11220)  
 5'-GCCBBBGBB CCBGCGCCBGC-3' (FRAG. NO:1839) (SEQ ID NO:11221)  
 70 5'-GTG CTC CGG TGG CTT TTT-3' (FRAG. NO:1289) (SEQ ID NO:10667)  
 5'-GCT TGT GTG CTC TGC TGT CTC TG-3' (FRAG. NO:1290) (SEQ ID NO:10668)  
 5'-TTC CTT CCG GTG GTT TCT TCC TGG CTC TTG TCC T-3' (FRAG. NO:1291) (SEQ ID NO:10669)  
 5'-TTC TCT TGG CCC TTG GCC C-3' (FRAG. NO:1292) (SEQ ID NO:10670)

5'-GBTGTTTGT BCCBBBGBCT CBBGBBTTGCT TTTGCTBTCT BBGGBTBCB TTTBGBCBT GBBBBCGCT GTBGGTCBGBB  
BGBTGCTT BCCTTCBCB BGBGCTGCB BBTBGBBGG CTGCCBBGBG CBCCGCCBGC TTGGBGTCT GTTTBCBCB  
BGTBGGTGC TCCGGTGGCT TTTGCTGT-3' (FRAG. NO:1840) (SEQ ID NO:11222)

**Human IL-8 Receptor Alpha Antisense Oligonucleotide Fragments**

- 5 5'-ACAGGGGCTG TAATCTTCATC TGCAGGTGGC ATGCCAGTGA AATTAGATC ATCAAAATCC CACATCTGTG GATCTGTAAT  
ATTTGACATG TCCTCTTCAG TTTCAGCAAT GGTGTGATCT AACTGAAGCA CCGGCCAGGB CBGGGGCTGT BBTCTTCBTC  
TGCBGGTGGC BTGCCBGTGB BBTBGBTC BTCCBBBTCC CBCBTCTGTG GBTCGTBBT BTBGBCBT TCCTCTCBG  
TTTCBGBB TGGTTTGBTC TBBCTGBGC BCCGGCCBGG TGGCTCGGTG CTCTGCCCC TGTGTGCG GCGCTCGGT  
GGTGTGGCC...CTGTGGTGT TCGTTCCCC CTCTTCTCT TGTTCGGGG...GTTCTGTGG CGGGTGCTT GTCTCGTTCC-  
3'(FRAG.NO:1841)(SEQ ID NO:11223)
- 10 5'-CBGGGGC-3' (FRAG. NO:1842) (SEQ ID NO:11224)  
5'-GCBGGTGGC-3' (FRAG. NO:1843) (SEQ ID NO:11225)  
5'-GCGGGCGTC-3' (FRAG. NO:1844) (SEQ ID NO:11226)  
5'-TGGCTCGGTGCTCTGCCCC (FRAG. NO:1293)(SEQ ID NO:10671)  
15 5'-TGTGTGTGCGGCGCTC (FRAG. NO:1294)(SEQ ID NO:10672)  
5'-GGTGGTGTGCGCCCTG (FRAG. NO:1295)(SEQ ID NO:10673)  
5'-TGGTGTCTCGTTCC (FRAG. NO:1296)(SEQ ID NO:10674)  
5'-CCCTCTTCTCTTTGTTC (FRAG. NO:1297)(SEQ ID NO:10675)  
5'-GGGGTCTTGTGTGC (FRAG. NO:1298)(SEQ ID NO:10676)  
20 5'-GGGCTGCTGTCTCGTTCC (FRAG. NO:1299)(SEQ ID NO:10677)  
5'-ACAGGGGCTG TAATCTTCATC TGCAGGTGGC ATGCCAGTGA AATTAGATC ATCAAAATCC CACATCTGTG GATCTGTAAT  
ATTTGACATG TCCTCTTCAG TTTCAGCAAT GGTGTGATCT AACTGAAGCA CCGGCCAGG-3' (FRAG. NO:1845) (SEQ ID NO:11227)  
5'-B CBGGGGCTGT BBTCTTCBTC TGCBGGTGGC BTGCCBGTGB BBTBGBTC BTCCBBBTCC CBCBTCTGTG GBTCGTBBT  
BTBGBCBT TCCTCTCBG TTTCBGBB TGGTTTGBTC TBBCTGBGC BCCGGCCBGG-3' (FRAG. NO:1846) (SEQ ID NO:11228)
- 25 Interleukin-11 (IL-11) Nucleic Acid and Antisense Oligonucleotide Fragments  
5'-GCTCAGGGCA CATGCTCCC CTCCCCAGGC CGCGGCCAG CTGACCCTCG GGGCTCCCC GGCAGCGGAC AGGGAAGGGT  
TAAAGGCCCC CGGCTCCCTG CCCCTGCC TGGGGAACCC CTGGCCCTGT GGGGACATGA ACTGTGTTG CCGCCTGGTC  
CTGGTCTGTG TGAGCTGTG GCCAGATACA GCTGTGCC CTGGGCCACC ACCTGGCCCC CCTCGAGTTT CCCCAGACCC  
30 TCGGGCCGAG CTGGACAGCA CCGTGTCTCT GACCCGCTCT CTCTGGCGG ACACGCGGCA GCTGGCTGCA CCGCTGAGGG  
ACAAATCCC AGCTGACGGG GACCACAACC TGGATTCCCT GCCACCCCTG GCCATGAGTG CCGGGGCACT GGGAGCTCTA  
CAGCTCCAG GTGTGTGAC AAGGCTGCGA GCGGACCTAC TGTCTACCT GCGGCACGTG CAGTGGCTGC GCGGGCAGG  
TGGCTCTTCC CTGAAGACCC TGGAGCCGA GCTGGGCACC CTGCAGGCC GACTGGACCG GCTGCTGCGC CGGCTGCAGC  
TCCTGATGTC CCGCTGGCC CTGCCCAGC CACCCCGGA CCGCGCGCG CCGCCGCTGG CCGCCCCCTC CTCAGCTGG  
GGGGCATCA GGGCCGCCA CGCCATCTG GGGGGCTGC ACCTGACACT TGAAGGGGAC GTGAGGGGAC TGCTGTGCT  
35 GAAGACTCG CTGTGACCCG GGGCCCAAG CCACCACCGT CCTTCCAAAG CCAGATCTTA TTTATTTAT TATTTAGTA  
CTGGGGCGA AACAGCCAGG TGATCCCCC GCCATTATCT CCCCTAGTT AGAGACAGTC CTTCGTGAG GCTGGGGGA  
CATCTGTGCC TTATTTATAC TTATTTATTT CAGGAGCAGG GGTGGGAGG AGGTGGACTC CTGGTCCCC GAGGAGGAGG  
GGAGTGGGT CCGGATTCT TGGGTCTCCA AGAAGTCTGT CCACGACTT CTGCCCTGGC TCTTCCCCAT CTAGCTCGG  
GCAGGAACAT ATATTATTA TTAAGCAAT TACTTTTAT GTTGGGTGG GAGCGAGGG GAAAGGGAAG CTCGGGTTT  
40 TGTACAAAA TGTGAGAAAC CTTTGTGAGA CAGAGAACAG GGAATTAAT GTGTCATACA TATCC CAGCTGCGGC  
ATCCTCTGTC TCAGAGTCTT GGTGTCTCTG TTCTTTCCC CTGGGGTCT CCCTGGGTCT CCCCAGTCC CTCCTGCTGT  
CTTCTCCCG CTCTCTGATC TCTGACTCC AGAACCTCT CCTCTGTCT CAGGGCTGCC CCTCTGATCT TCTTGTCTT  
TCTGGTGTG CTCTCTGGCT GCCTCCATCT CCGTCTCCCT GTCTCTGTCT CAGTCTGTCT GCTCTGCTCT  
45 GTGTGTGTG GTCTCTCTCT CTCTCTCTC TTCCCTTCCA CTCCCTCTC CTCTGCTC CACCTCTCCA GCGCCCTGTC  
TTGTCCCTCC GTCCGGCTT TCTCTGCCCT TCGTCTCTG TGCTCCCCA TCTCTCTCTG CTAGTCTCTG CCAGCGGAC  
CCCCACCCAC AGTGGGGCC CAGCGCTTGA GCCTGATGT CTGTCCCGC CCGTGGAGGT GAGGGGAGG GACGCCAATG  
ACCTACCCAG CCCCCTCCG ACCACCCCC CCTTTCCCT TTCAACTTTT CCAACTTTT CTTCGTGCC CTCCTCCGAG  
CGCGCGCGG TGAGCCCTGC AAGGCAGCCG CTCGTCTGA ATGGAAGAG CAGGCAGGGA GGGTGAGTCA GGATGTGTA  
GGCGGGCCCT CCCCCTGCC CTGCCCCCC CGCGCCCGC CCAGGCCCCC TATATAACCC CCCAGGCGTC CACACTCCCT  
50 CACTGGCGG GCGCTCTGCT CTCAGGGCAG ATCGCTCCC TCCCGACGCC CGGGCCGAGC TGACCTCGG GGCTCCCCG  
GCAGCGGACA GGAAGGGTT AAAGGCCCCC GGCTCCCTGC CCGTGGCTT GGGGAACCC TGGCCCTGTG GGGACATGAA  
CTGTAAAGTT GTTCATGGG AGGGTGGAG GACAGGGAG GCAGGGAGGA GAGGGACCCA CCGCGGGGGT GGGAGCAGAC  
CCCGTGAGT CGACAGAGA GGGACCCGA GACAGGAGC CGGGGAGGAG AGCAGCTTCG GAGACAGGAG GCGCGGAGG  
AGATGGGAG AGACAGACAG AGACAGGAGC GGATGGAGG AGCAATCAG AGGCGCCGA GAGGAGACCG GCCAGACAG  
55 GCGGAGAGG AGCGAGACGC GAGACCGAGC AGGGGAGGAG ACAGAGGAG TGGTGCCGG AGGGAGGTGA CCCCCATCGA  
CCCGAGCCCC AGGGAGCCG CCGGGAGCCG GAGACTCCCT GGGATTCCG CAGAGAGGCT CCGGAGGGAA ACTGAGGAG  
GGTCCCGGA GAGCGGAGCA AGCCAGGGAG TAGCGACCC AGCCGGGGG AGGAGAGAGA CTGGGCGCC GGGGAAGCG  
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60 CGAGCTCCG ACCCCGCGC CCCCAGCGC CCGCGGCCG CCGCGGCCA GCTCTCCG TCCCGCGCC CGGCGGGG  
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65 AGCCGCGCTG GCGCTGCGAC CTGCGCGCG CTGGTCCACC CTGGGACTTA AGACCTCCAG CTCACTCTC CTAAAGCCG  
GGAGTCCAG CCCCAGACCC TCCTCCCGA GACCCAGGAG TCCAGACCC AGGCTCTCT CCTCAGAC TAGGAGTCCA  
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70 GGCGAGCTG GACAGACCG TGCTCTGAC CCGCTCTCT CTGGCGGACA CCGGCGAGT GGCTGACAG CTGTTAGGAG  
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ACCCTGGCA TGAGTGCAG GCACTGGA GCTCTACAG TAAGGGCAAG GAGTGGGCT GGGGACAAG TGGAGGCGAG  
75 GCACTGAAG GGGCGGGAG GATGAGGGC ACTGTCGGG GTTCTCTGA TGTCCCGCT CTATCCCCAG CTCCAGGTG

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 TGGCCCCAAG ACCTGACACC CCAGACCCCC CCAGCTGGCC CCAAAAATCT GTGGCCTGAG TCCTTTGAAGC CTGAGACCCC  
 5 AGACCCGAGT GCAACAGCCC CGCTCTGAGA CCTGACACC CTAACAGCCC GCTCTGAGAC CCTGACACCG TAACAGCCCC  
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 AGGCCCTAGA CCCCCAAATC CTGCCCAGAA ACTTCAAATT CTCACCCAAG ACCCTGAGAC TCCATCATCC ATGACCTCAA  
 AGTCCCCAGA TCCCCAGCCC TAAGACCCAA GACCCCATCC TGAAGCCCAA AGCCTTGAGA ATTCAAATCC TCACCTCAAG  
 ACTTGGAGAC CCTGGCCCCA TGACATTGAA AACCATGGAC CTGCCCAGGC GTGGTGGCTC ACGCCTGTAA TCCCAGCACT  
 TTGGGAGGCC GAGGCAAGTG GATCACCTGA GGTGCGGAGT TCAAGACCAG CCAGACCAAC ATGGTGA AAC CTGTCTCTA  
 10 CTAAAAATAG AAAATTAGCC AGGCGTGGTG GTGCATGCCT GTAATCCCAG CTACTTGGGA GGCTGAGGCA GGAGAATCGC  
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 CTGTACAAAC CCAAGACCTC CAGGACCTAG ACCCGGACCC ATGTCTCACT CCCAACCTG CCCAACCTGA  
 15 CACCTCAGAT CCTGAGCCTG CGCCTGTACG ACTCCAAGAC CCTCACTTCC AAAGCCAGGC CCAAAGCCCT GAGACCGAGAA  
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 25 CTCACCTAGA ACCGAGATGC CAGCCCTGAC TCCACGACT TCACCCCAA CCCCACACT CAGCTCTGGA AGCCCGTCT  
 GACTCCAGCC TCCATTTTCG GAACCCACA GCTGAAAGAG CTCCCGGCT AAACACTTCA CCCCACGCGC CACAGTCCCC  
 CTGTGAATAT GCAGCCCCGA TTCAGCTGCA GCTCCACAGC ACCCTGCCC TGCACCCCG CTGCACCCCT TACCTGTGAC  
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 30 CCCCCCTCT CAGCCTGGGG GGGCATCAGG GCGGCCACG CCATCCTGGG GGGGCTGCAC CTGACACTTG ACTGGGCCGT  
 GAGGGGACTG CTGCTGCTGA AGACTCGGCT GTGACCCGGG GCCCAAAGCC ACCACGCTC TTCCAAAGCC AGATCTTATT  
 TATTTATTTA TTTCAGTACT GGGGGCGAAA CAGCCAGGTT ATCCCCCGC CATTATCTCC CCCTAGTTAG AGCAGTCTCT  
 TCCGTGAGGC CTGGGGGCA TCTGTGCTT ATTATATCT TTATTATTTA GGAGCAGGGG TTGGAGGCGAG GTGGACTCT  
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 35 AAGGGAAGCC TGGGTTTTTG TACAAAAATG TGAGAACACT TTGTGAGACA GAGAACAGGG AATTAATGT GTCATACATA  
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 45 ATATCCAACA GTGAGGGTTA AGCAACATGG TGATCTGTG GATAGAACGC CACCCAGCCG CCGGAGGAGC GGACTGTCTAT  
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 AACCTGTCT CAAAAAAGAA AGAATGATGT CCTGACATGA AACAGCAGGC TACAAAACCA CTGCATGCTG TGATCCCAAT  
 TTTGTGTTTT TCTTTCTATA TATGGAITAA AACAAAAATC CTAAAGGGAA ATACGCCAAA ATGTTGACAA TGACTGTCT  
 50 CAGGTCAAAG GAGAGAGGTG GGATTTGGG TGACTTTTAA TGTGTATGAT TGTCTGTATT TTACAGAAIT TTAGCCATGA  
 CTGTGTATT TGCATGACAT ATTTTAAAAA TAATAAACAC TATTTTAGA ATAACAGAA ATCAGCCTCC TCCTCTCCAA  
 AAATAAGCCC TCAGGAGGGG ACAAAGTTGA CGCTGATTG AGCCTGTGAG GGTGTGAC-3' (FRAG. NO. 11892)  
 5'-GCTCAGGGCA CATGCTCTCC CTCCCAGGC CGGGGCCAG CTGACCCTCG GGGTCCCCC GGCAGCGGAG AGGGAAGGGT  
 TAAAGGCCCC CGGCTCCTG CCCCCTGCC TGGGGAACCC CTGCGCCTGT GGGGACATGA ACTGTGTTT GCGCTGTGTC  
 55 CTGGTCTGTC TGAGCCTGTG GCCAGATACA GCTGTGCCCC CTGGGCCACC ACCTGGCCCC CCTCGAGTTT CCCCAGACCC  
 TCGGGCCGAG CTGGACAGCA CCGTGCTCCT GACCCGCTCT CTCTGGCGG ACACGCGGCA GCTGGCTGCA CAGCTGAGGG  
 ACAAATTCCT AGCTGACGGG GACCACAACC TGGATTCCCT GCCCAGCTG GCCATGAGTG CCGGGGCACT GGGAGCTCTA  
 CAGTCCCAAG GTGTGCTGAC AAGGCTGCGA GCGGACCTAC TGTCTACCT GCGGACGTC CAGTGGCTG CCGGGCAGG  
 TGGCTCTTCC CTGAAGACCC TGGAGCCGA GCTGGGCACC CTGCAGGCC GACTGGACCG GCTGCTGCGC CGGCTGCAGC  
 60 TCCTGATGTC CCGCTGGCC CTGCCACAG CACCCCGGA CCGCGCGCG CCCCCTGCG CCGCCCCCTC CTCAGCCTGG  
 GGGGGCATCA GGGCCGCCA CGCCATCCTG GGGGGCTGC ACCTGACACT TGACTGGGCC GTAGGGGAC TGCTGTGCT  
 GAAGACTCGG CTGTGACCCG GGGCCCAAAG CCACCACCGT CCTTCCAAAG CCAGATCTTA TTTATTTATT TATTTAGTA  
 CTGGGGGCGA AACAGCAGG TGATCCCCC GCCATTATCT CCCCCTAGTT AGAGACAGTC CTTCGTTGAG GCCTGGGGGA  
 CATCTGTGCC TTATTTATAC TTATTTATT CAGGAGCAGG GGTGGGAGGC AGGTGGACTC CTGGGTCCC GAGGAGGAGG  
 GQACTGGGT CCGGATTCT TGGGTCTCCA AGAAGTCTGT CCACAGACT CTGCCCCTGC TCTTCCCAT CTAGCCCTGG  
 65 GCAGGAACAT ATATTATTTA TTTAAGCAAT TACTTTTCAT GTTGGGTGG GAGCGGAGG GAAAGGGAAG CCTGGGTTTT  
 TGTACAAAAA TGTGAGAAAC CTTGTGAGA CAGAGAACAG GGAATTAAT GTGTCATACA TATCC-3' (FRAG. NO. 11890)  
 5'-CAGCTGCGGC ATCTCTGTC TCAGAGTCTT GGTGTCTCTG TTCTTTTCCC CTGCGGGTCT CCCTGGGTCT CCCCAGTCC  
 CTCTGCTGT CTCTCTCCG CTCTCTGATC TCTGACTCC AGAACCTCTC CCTCTGTCTC CAGGCTGCTC CTCTGATCC  
 70 TCTTTGCTT TCTGGTGTGT CTCTCTGGT GCCTCATCT CTGTGGATCT CCGTCTCCCT GTCTCTGCT CAGTCTGTCC  
 TTAATCTGT GTGTGTGTGT GTCTCTCTCT CTCTCTTCC TCCCTTCCA CTCCCTCTC CTCTGCTC CACCTCTCCA  
 GGGCCCTGTC TTGTCCCTCC GTCCGGCCTT TCTCTGCTT TCCGTCTCC TGCTTCCCA TCTCTCTCT CTAGTCTGT  
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 GACGCCAATG ACCTCACCAG CCCCCTCCG ACCACCCCG CTTTCCCTT TCAACTTTT CCAACTTTT CTCCGTGCC  
 75 CTCCTCCAG CGCGCGCGG TGAGCCCTG AAGCGAGCC CTCCGTCTGA ATGGAAGAG CAGGCAAGGA GGTGAGTCA

GGATGTGTCA GGCCGGCCCT CCCTGCGCG CTGCCCCCG CCCGCCCGCC CCAGGCCCCC TATATAACCC CCCAGGCGTC  
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 GGCTCCCCCG GCAGCGGACA GGAAGGGTTT AAAGGCCCCC GGCTCCTGCG CCCCTGCCCT GGGGAACCCC TGCCCTGTG  
 5 GGGACATGAA CTGTAAAGTTG GTTCATGGGG AGGGTGGAGG GGACAGGGAG GCAGGGAGGA GAGGGACCCA CGGCGGGGGT  
 GGGAGCAGAC CCCGCTGAAT CGCACAGAGA GGGACCGGA GACAGGCAGC CGGGGAGGAG AGCAGCTTCG GAGACAGGAG  
 GCGGCGGAGG AGATGGGCAG AGAGAGACAC AGACACTGAG GGATGGAGGC AGCCAATCAG AGGCCCGCA GGAGGGACGG  
 GCCAGAGAGG GCCCGAGAGG AGCGAGACGC GAGACCGAGC AGGGGAGGG ACGCAGGGAC TGGTGCCGGG AGGGAGGTGA  
 CCCCCATCGA CCCAGGCCCG AGGGAGCCCG CGGGGACCGG GAGACTCCCT GGGATTCCGG CAGAGAGGCT CCGGAGGGAA  
 10 ACTGAGGCAG GGTCCGCGGA GAGCGGAGCA AGCCAGGGAG TAGCGACCCC AGCCGGGGGG AGGAGAGAGA CTGGGCGCGG  
 GGGGAAAGCG AGCGAGAGCG GGCAGATGCG GCGGACGGAG GCGCGGACAG ACCGACGGCT GCGCGGCCCG GGGGCGGGC  
 TGGGGGTGTG CGAGGCGCGG GCGGCGGGG AGCGCTGATT GGCTGGCGGG TGGCCGGGTG GCGGGGGCGG CCGGGGTGGG  
 CTGCGGGGAG CGAGCTCCGG ACCCGCGCGC CCCCGCGGCC CCCCGCGGCC CCGCGCGCCA GCTCTCCCGC TCCCGCGCGC  
 CGGCGGGGCG ATGGCTCTGC CCTCTCCCG CCAGGTGCGC TGCGGCGCGG GCTTCTGCGG CCCACCGCG GGGCTCTGG  
 15 GAGGGCGTCT AAGGGGTCTC CCGTGGGAGA GTGCTGTGTC TCCCGGACTC CGTCTGGGGC TTTTGGCTCC TTTCCCTGCT  
 CCCAGCCAGC TCGGGCTCCC GCGGCGCGGG GAGGGGGCAG GTTCTGGGCT GTGCTCCCG CACCATCCCG GCGCGGGGGC  
 CCAGATTCCG GCGTCCGGGG GCGGACGGGA GACGCGCGGG CCGGCTGCTG TCCGACGGGC GGGGACGCA GAGCCAGGGA  
 GGGAGAGGGA AGCCCGCCTG GCCCTGCGAC CTGCGCGGG GCGTTCCACC CTGGGACTTA AGACCTCCAG CTCCATCCTC  
 CCTAAGGCCG GGAGTCCAGG CCCCAGACCC TCTTCCCGA GACCCAGGAG TCCAGACCCC AGGCCCTTCT CCCTCAGACC  
 20 TAGGAGTCCA GGGCCCCAGC CTCTCCTCCC TCAGACCCAG GAGGAGTCCA GACCCAGATT CCTCCTCCCT CAGACCCGGG  
 AGTCCAGCCC AGGCCCTCTT CTCTCAGACC CGGAGTCCAG CTTGAGCTCT CTGCCCTATC CTGCCCCAG GTGTTTGCCG  
 CCGTGTGCTG TCGTGTGCTC GCGTGTGCG AGATACAGCT GTGCGCCCTG GGGCCACACC TGGCCCCCTT TGGCTTTCCC  
 CAGACCTCTG GCGCGAGCTG GACAGCACCG TGCTCTGAC CCGCTCTCTC CTGCGGACA CGCGGACGCT GGCTGCACAG  
 CTGGTAGGAG AGACTGGGCT GGGGCCAGCA CAGGAGTGA AGGCAGAGAG GAACGGAGAG GAGTCTGCGG GCAGCCACTT  
 GGAGGGTTTC TGGGCTCTCA GGTGGCAGAG TGAGGGAGGG AAGAGTTGG GGGCTGGCG TGGGGAGTGG AGGAGGCCCG  
 25 GAGGCTGGGC AGGGGCCACC TCACAGCTTT TTTCCCTGCC AGAGGGACAA ATTCCAGCT GACGGGGACC ACAACTGGA  
 TTCCCTGCCC ACCCTGGCCA TGAGTGACAG GGCAGTGGGA GCTCTACAG TAAGGGCAAG GGAGTGGGCT GGGGACAAGG  
 TGGGAGGCGA GCACTGAAGG GGGCGGGGAG GATGAGGGGC ACTGCTCGGG GTTCTCTGA TGTCCCGGT CTATCCCCAG  
 CTCCAGGCTG TGTGACAAAG GCTGCGAGCG GACTACTGCT CCTACTGCG GCACGTGACG TGGCTGCGCC GGGCAGCTGG  
 30 CTCTTCCCTG AAGACCTTG AGCCCGAGCT GGGCACCTCG CAGGCCCGAC TGGACCGGCT GCTGCGCGG CTGCAGCTCC  
 TGGTATGTCC TGGCCCCAAG ACCTGACACC CCAGACCCCG ACCCTGGGCC CCAAAATCCT GTGGCTGAG TCCTTGAAGC  
 CTGAGACCCC AGACCCGAGT GCAACAGCCC CGCTCTGAGA CCTTGACACC TTAACAGCCC GCTCTGAGAC CCGTACACCG  
 TAACAGCCCC GCTCTGAGAC CCGTGAACCTA ACAGTCTGCA TCTGAGACCC TGACCCCTGCA GTCCCAAGAT CTGTGGCCC  
 TGAGACCTTG AGGCCCTAGA CCCCCAAATC CTGCCAGAA ACTTCAAAAT CTCACCCAAG ACCCTGAGAC TCCATCATCC  
 ATGACCTCAA ACTCCCGAGA TCCCAGCCCC TAAGACCCAA GACCCCATCC TGAAGCCCAA AGCCTTGAGA ATTCAAATCC  
 35 TCACCTCAAG AGTTGGAGAC CCGTGCCCCA TGACATTGAA AACCATTGGC CTGGCCAGGC GTGGCTGCTC AGCCTGTAA  
 TCCCAGCACT TTGGGAGGCC GAGGCAAGTG GATCACTGA GGTGCGGAGT TCAAGACCAG CCAGACCAAC ATGGTGAAAC  
 CCTGTCTCTA CTAAAAATAG AAAATTAGCC AGGCGTGTGT GTGATGCTT GTAATCCAG CTAATTGGGA GGCTGAGGA  
 GGAGAAATCCG TTGAACCTTG GAGGCGGAGG TTGCACTGAG CCGAGATGCG ACCATTACAC TCCAGCCTGG GCAACAAGAG  
 40 CAAAACCTCCC TCTCTCTCAA AAAAAAATAA AAAAAAATAA AAGAAAGGAA AGAAAAACCAT GGACCTCCAG ACCCTGAGAC  
 CCCAGGCCCG AGCCCTGAGA TCCTGACATC TTAAGATCC CAGGCCCTAA GATACAAGAC CTTGACCCAA AGCCAGCCTT  
 GGGACCCCTG CTGTACAAAC CCAAGACCTC CAGGACCTAG ACCCGAGGCC CTGAGGCCCT ATGTCTCACT CCAACATCG  
 AAAACCTGAG GACCTCAGAT CCGTGAACCTG CGCTCTGAG ACTCCAAGAC CTTCACTTCC AAAGCCAGGC CAAAAGCCTC  
 GAGACCAAGAA GACTTCAAAC CCTGTTCTT GGGCTAACT CCAAAGACCC TGGATCTCAA ATTCCAATT CTAGCTCTGA  
 45 GACTCCAGCC CTCACCATG AGTTCTGAA CTGGAACCA GAGACCCCAT CTCTAAGACT TCAGCCTGA GATCCAGGGC  
 CTGACCTTAG ACTCGAGCCC ACAGACCTCA GATACTGTCT GTAAAAACCC AGCTCTGGTG GGGAGCAGTG GCTCACTCT  
 GTAATCCCAA GGCAGGGGAG GCCAAGGCAG AAGGACCTCT TGAGGCCATG AGTTTGAGAG AGCCTGGGCA GCATAGCAA  
 ACTCTGTTTC TTAATTATTA TTATTATTAT TATTTTTTGG AGACAGAGTC TCGCGCTCTG TTGCCAGGC TAGAGTGCAA  
 TGGTGCCATT TCGGCTTGCT GGAACCTCCG CCTCTGGGG TCAAGCGATT CTCTGCTC AGCCTCTGA GTAGCTGGGA  
 50 CTTCAGGTGC ACATGCCAC ACCCGATAA TTTTITGTGA TTTTAGTGA CACAGGGTTT CACCGTGTG CCAAGCTGG  
 TCACAAACTC CTGAGCTCAG GCCATCCGCG CGCTCTGGCC TCCCAAGCG CTGGGATAAC AGGCGTGACG CCGCGCTGG  
 CTTCTTAATT GTTCTAACAG CAGCGACAAC AACAAAAACC CAGCTCTGAG ATTCCAGCCC CGGCGACTCT AACAGTCCA  
 GGCCCGATCC CTCACCTAGA ACCGAGATGC CAGCCCTGAC TCCACAGACT TCACCCCAA CCCCCACAT CAGCTCTGGA  
 AGCCCGCTCT GACTCCAGCC TCCATTTCG GAACCCACA GCGCTGAAGAG CTCCCGGCC CTCCAGCTCA CCGTACGCGC  
 55 CACAGTCCCC CTGTGAATAT GCAGCCCCGA TTCAGCTGCA GCTCCACAGC ACCCTGCGCC TGCACCCCG CTGCACCCCG  
 TACCTGTGAC TCACCTCTCT CCTCTCCCA CAGATGTCCC GCTTGGCCCT GCGCCAGCCA CCGCGGACC CGCGCGCGC  
 CCGCTGCGG CCCCCCTCT CAGCTGGGG GGGCATCAGG GCGGCCACG CCATCCTGGG GGGGCTGCAC CTGACACTTG  
 ACTGGGCGGT GAGGGGACTG CTGCTGCTGA AGACTCGGCT GTGACCCGGG GCGCAAAGCC ACCACGCTC TTCCAAAGCC  
 AGATCTTATT TATTTATTTA TTTCAGTACT GGGGGCGAAA CAGCCAGGTG ATCCCCCGC CATTATCTCC CCTAGTTAG  
 AGACAGTCTT TCCGTGAGCG CTGGGGGGCA TCTGTGCCTT ATTTATACTT ATTTATTTCA GGAGCAGGGG TGGGAGGCAG  
 60 GTGGACTCCT GGGTCCCGA GAGGAGGGG ACTGGGGTCC CGGATTCTTG GGTCTCCAAG AAGTCTGTCC ACAGACTTCT  
 GCCCTGGCTC TTCCCATCT AGGCCTGGG AGGAACATAT ATTATTTATT TAAGCAATTA CTTTTCATGT TGGGGTGGGG  
 ACGGAGGGGA AAGGGAAGCC TGGGTTTTT TACAAAAATG TGAGAAACCT TTGTGAGACA GAGAACAGGG AATTAATGT  
 GTCATACATA TCCACTTGAG GGCATTTGT CTGAGAGCTG GGGCTGGATG CTTGGGTAACT TGGGGCAGGG CAGGTGGAGG  
 65 GGAGACCTCC ATTCAAGTGG AGGTCCCGAG TGGGCGGGG AGGCATGGG AGATGGGTG AGTACCCAGA CAGCTCTGTG  
 GAGGCAGGGT CTGAGCCTTG CCTGGGGCCC CGCACTGCAT AGGGCCGTTT GTTTGTTTTT TGAGATGGAG TCTCGCTCTG  
 TTGCTAGGC TGGAGTGCA TGAGGCAATC TAAGGTCACT GCAACCTCCA CCTCCCGGT TCAAGCAATT CTCTGCCCT  
 AGCCTCCCGA TTAGCTGGGA TCACAGGTGT GCACCACTAA GCGGAGCTAA TTATTTATTT CTTTGTATT TTTAGTAGAG  
 ACAGGGTTTC ACAGGTGTTG CCAGGCTGGT TTCGAACCTC TGACCTCAGG TGATCCTCT GCCTCGGCT CCAAAAGTGC  
 TGGGATTACA GGTGTGAGCC ACCACACCTG ACCCAATAGT CTCAATAAAA TATTTAATGG AAGGTCCAC AAGTACCCCT  
 70 GTGATCAACA GTACCCGTAT GGGACAAAGC TGCAAGGTCA AGATGGTTCA TTATGGCTGT GTTCACCATA GCAAACTGGA  
 AACAATCTAT ATATCAACA GTGAGGGTTA AGCAACATGG TGATCTGTG GATAGAACCG CACCCAGCGC CCGGAGCGAG  
 GGACTGTCTAT TCAGGGAGGC TAAGGAGAGA GGCTTGCTTG GGATATAGAA AGATATCCTG ACATTGGCCA GGCATGGTGG  
 CTCACGCGCT TAATCTGGC ACTTTGGGAG GACGAAGCGA GTGGATCACT GAAGTCCAAG AGTTTGAGAC CGGCCTGCGA  
 GACATGGCAA AACCTGTCT CAAAAAGAA AGAATAGTGT CCGTACATGA AACAGCAGGC TACAAAACCA CTGACTGCTG  
 75 TGATCCCAAT TTTGTGTTTT TCTTCTATA TATGGATTAA ACAAAGGAA ATACGCCAAA ATGTTGACAA

TGACTGTCTC CAGGTCAAAG GAGAGAGGTG GGATTGTGGG TGACTTTTAA TGTGTATGAT TGTCTGTATT TTACAGAATT  
TCTGCCATGA CTGTGTATTT TGCATGACAC ATTTTAAAAA TAATAAACAC TATTTTATAGA ATAACAGAAT ATCAGCCTCC  
TCTCTCCAA AAATAAGCCC TCAGGAGGGG ACAAAGTTGA CCGCTGATTG AGCCTGTCAAG GGCTGTGCAC-3' (FRAG. NO: ) (SEQ  
ID NO:11891)

#### 5 Human GM-CSF Nucleic Acid and Antisense Oligonucleotide Fragments

5'-CTTGBGCBGG BBGCTCTGGG GCBGGGBGCT GGCBBGGGCC BGGGGGGTGG CTTCCTGCBC TGTCCBGBGT GCBCTGTGCC  
BCBGCBCBGG CTGCBGGGCC BTCBGCTTCB TGGGGCTCTG GGTGGCBGGT CCBGCCBTGG GTCTGGGTGG GGCTGGGCTG  
CBGGCTCCGG GCGGTCCBGGCBTGGGTCTG GGGGCTGGG CTGCBGGCTC CGGGCGGGCG GGTGCGGGCT GCGTGTGGG  
GGCTGCCCGG CAGGCCCTGC GGTCCBGGCB TGGGTCTGGG GGCTGGGCTG CBGGCTCCGG GCGGGCGGGT GCGGGCTGCG

10 TGCTGGGGG TGCCCCGAC GCCCTGC-3' (FRAG. NO:1847) (SEQ ID NO:11229)

5'-GBGCBGG BBG-3' (FRAG. NO:1848) (SEQ ID NO:11230)

5'-GCCBCBGBGCBGC-3' (FRAG. NO:1849) (SEQ ID NO:11231)

5'-GGG TGC GGG C-3' (FRAG. NO:1850) (SEQ ID NO:11232)

5'-GGT CCB GCC BTG GGT CTG GG-3' (FRAG. NO:1300) (SEQ ID NO:10678)

15 5'-GGC TGG GCT GCB GGC TCC GG-3' (FRAG. NO:1301) (SEQ ID NO:10679)

5'-GCG GGC GGG TGC GGG CTG CGT GCT GGG-3' (FRAG. NO:1302) (SEQ ID NO:10680)

5'-GGC TGC CCC GCA GGC CCT GC-3' (FRAG. NO:1303) (SEQ ID NO:10681)

5'-CTTGBGCBGG BBGCTCTGGG GCBGGGBGCT GGCBBGGGCC BGGGGGGTGG CTTCCTGCBC TGTCCBGBGT GCBCTGTGCC  
BCBGCBCBGG CTGCBGGGCC BTCBGCTTCB TGGGGCTCTG GGTGGCBGGT CCBGCCBTGG GTCTGGGTGG GGCTGGGCTG  
CBGGCTCCGG GC-3' (FRAG. NO:1851) (SEQ ID NO:11233)

#### 20 Human Tumor Necrosis Factor ( Antisense Oligonucleotide Fragments

5'-GCBCCGCTG GBGCCCTGGG GCCCCCCTGT CTCTTGGGG BGGCCCTCCT CGGCCBGTCT CBCGTCCCGG BTCBTGCTTT  
CBGTGCTCBT GGTGTCTTTT CCBGGGGGBG GBGGGGCTGG TCCTCTGCTG TCCTTGCTGG TGCTCBTGGT GTCCTTTCCG  
CCCTGGGGCC CCCTGTCTT CTGGGGGCTT CTTCCTCTG GGGGCCGTCT CTCTCCCTCT CTTCGCTCTC TCTCTTCTC  
25 TCTCTCTCT CCCCTTTCCC GCTCTTCTG TCTCGGTGTC TGTGTTTCTC TCTCCGCTGG CTGCGTGTCT GGCCTGGCT  
CTGGGCTGT GCTGTTCTC CTCCGGTTCC TGCTCTCTCT GTCTGTGCC CCCTCTGGGG TCTCCCTCTG GGTGGTGGTC  
TGTGCTTG GGTGGGCTC CGTGTCTCCB GTGCTCBTGG TGTCCGCTGB GGBGCGCTCT GCTGGCGCTG GTCCTCTGCTGTC  
CTTGCTGGTG CTGCTGGTGT CCTTTCCGCC CTGGGGCCCC CCTGTCTTCT TGGGGCCTCT TCCCTCTGGG GGCGGTCTC  
TCTCCCTCTC TTGCGTCTCT CTCTTCTCT CTCTCTCTC CCCTTTCCCG CTCTTCTGT CTGCGTGTCT GGTGTTCTCT  
30 CTCCGCTGGC TGCCTGTCTG GCCTGCGCTC TTGGCCTGTG CTGTCTCTCC TCCGGTCTCT GTCTCTCTG TCTGTGCGCC  
CCTCTGGGGT CTCCCTCTGG CGTGGTGGTC TTGTGCTG GGTGGGCTC CGTGTCTCCB GTGCTCBTGG TGTCCGCTGB  
GGBGCGCTCT GCTGGC-3' (FRAG. NO:1852) (SEQ ID NO:11234)

5'-GGGGCCCCC-3' (FRAG. NO:1853) (SEQ ID NO:11235)

5'- GGG GGC CG TCT-3' (FRAG. NO:1854) (SEQ ID NO:11236)

35 5'-CCBGGGGGBG GBGGGGCTGG-3' (FRAG. NO:1855) (SEQ ID NO:11237)

5'-GCBCCGCTG GBGCCCTGGG GCCCCCCTGT CTCTTGGGG BGGCCCTCCT CGGCCBGTCT CBCGTCCCGG BTCBTGCTTT  
CBGTGCTCBT GGTGTCTTTT CCBGGGGGBG GBGGG-3' (FRAG. NO:1304) (SEQ ID NO:10682)

5'-GCT GGT CCT CTG CTG TCC TTG CTG GTG CTC BTG GTG TCC TTT CC GCC CTG GGG CCC CCC TGT CTT CTT GGG G CCT  
CTT CCC TGT GGG GGC CG TCT CTC TCC CTC TCT TGC GTC TCT C TCT TTC TCT CTC TCT CTT CCC C TTT CCC GCT CTT TCT  
40 GTC TC GGT GTC TGG TTT TCT CTC TCC GCT GGT GTC TCT GGC CTG CGC TCT T GGC CTG TGC TGT TCC TCC GGT  
TCC TGT CCT CTC TGT CTG TC GCC CCC TCT GGG GTC TCC CTC TGG C GTG GTG GTC TTG TTG CTT GGG CTG GGC TCC GTG  
TCT C CBG TGC TCB TGG TGT CC-3' (FRAG. NO:1305) (SEQ ID NO:10683)

5'-GCT GBG GGB GCG TCT GCT GGC GCT GGT CCT CTG CTG TCC TTG CTG GTG CTC BTG GTG TCC TTT CC GCC CTG GGG CCC  
CCC TGT CTT CTT GGG G CCT CTT CCC TGT GGG GGC CG TCT CTC TCC CTC TCT TGC GTC TCT C TCT TTC TCT CTC TCT CTT  
45 CCC C TTT CCC GCT CTT TCT GTC TC GGT GTC TGG TTT TCT CTC TCC GCT GGC TGC CTG TCT GGC CTG CGC TCT T GGC CTG  
TGC TGT TCC TCC TCC GGT TCC TGT CCT CTC TGT CTG TC GCC CCC TCT GGG GTC TCC CTC TGG C GTG GTG GTC TTG TTG  
CTT GGG CTG GGC TCC GTG TCT C CBG TGC TCB TGG TGT CC GCT GBG GGB GCG TCT GCT GGC-3' (FRAG. NO:1306) (SEQ ID  
NO:10684)

5'-GCT GGT CCT CTG CTG TCC TTG CTG-3' (FRAG. NO:1655) (SEQ ID NO:11033)

50 5'-GTG CTC BTG GTG TCC TTT CC-3' (FRAG. NO:1656) (SEQ ID NO:11034)

5'-GCC CTG GGG CCC CCC TGT CTT CTT GGG G-3' (FRAG. NO:1657) (SEQ ID NO:11035)

5'-CCT CTT CCC TCT GGG GGC CG-3' (FRAG. NO:1658) (SEQ ID NO:11036)

5'-TCT CTC TCC CTC TCT TGC GTC TCT C-3' (FRAG. NO:1659) (SEQ ID NO:11037)

5'-TCT TTC TCT CTC TCT CTT CCC C-3' (FRAG. NO:1660) (SEQ ID NO:11038)

55 5'-TTT CCC GCT CTT TCT GTC TC-3' (FRAG. NO:1661) (SEQ ID NO:11039)

5'-GGT GTC TGG TTT TCT CTC TCC-3' (FRAG. NO:1662) (SEQ ID NO:11040)

5'-GCT GGC TGC CTG TCT GGC CTG CGC TCT T-3' (FRAG. NO:1663) (SEQ ID NO:11041)

5'-GGC CTG TGC TGT TCC TCC-3' (FRAG. NO:1664) (SEQ ID NO:11042)

5'-TCC GGT TCC TGT CCT CTC TGT CTG TC-3' (FRAG. NO:1665) (SEQ ID NO:11043)

60 5'-GCC CCC TCT GGG GTC TCC CTC TGG C-3' (FRAG. NO:1666) (SEQ ID NO:11044)

5'-GTG GTG GTC TTG TTG CTT-3' (FRAG. NO:1667) (SEQ ID NO:11045)

5'-GGG CTG GGC TCC GTG TCT C-3' (FRAG. NO:1668) (SEQ ID NO:11046)

5'-CBG TGC TCB TGG TGT CC-3' (FRAG. NO:1669) (SEQ ID NO:11047)

5'-GCT GBG GGB GCG TCT GCT GGC-3' (FRAG. NO:1670) (SEQ ID NO:11048)

#### 65 Human Leukotriene C4 Synthase Nucleic Acids and Antisense Oligonucleotide Fragments

5'-CTCGGTBGC GCGCTCBBB TCGGTGGGG CGGTGGTGBG CGGCGGCBBC CGCGBBGGC CCTGCGCGCC GBGBTCBCTG  
CBGGGBBBG TBGGCTTCB GCBGGBCTCC CBGGGGGGT BCBGCBGCCB GTBGBGCTBC CTCGTCTTC BTGGTBCGT  
CGGTGTGGT GCBGCGGGCTG TGTGTBBGG CBGGCTGGG CCCGTCTGCT GCTCCTCTG CCGCTCTGCT CTTC TGG TA  
CGGTGCTGT GGTGGCTCG GGTGGGCGG TGTGGGGCG CGCGGCTCG GCTCTCTTT CCCGGCTCCG  
70 CGGCCCGGGG GCCTGGTCT CCCTCGTCT TCBTGGTBCC G-3' (FRAG. NO:1856) (SEQ ID NO:11238)

5'-GCB GCBGGBC-3' (FRAG. NO:1857) (SEQ ID NO:11239)

5'-CCCGGCTCCG-3' (FRAG. NO:1858) (SEQ ID NO:11240)

5'-CGGCCCGGG GCC-3' (FRAG. NO:1859) (SEQ ID NO:11241)

5'-CB CGCGG-3' (FRAG. NO:1860) (SEQ ID NO:11242)

5'-GCC CCG TCT GCT GCT CCT CGT GCC G-3' (FRAG. NO:1307)(SEQ ID NO:10685)  
 5'-CCT CGT CCT TCA TGG TAC CGT CGG TGT GGT GGC-3' (FRAG. NO:1308)(SEQ ID NO:10686)  
 5'-CTC GGG TGG GCC GGT GGT G-3' (FRAG. NO:1309)(SEQ ID NO:10687)  
 5'-GGG CGC GCG CGC TCG CGT-3' (FRAG. NO:1310)(SEQ ID NO:10688)  
 5'-GGC TCC GGC TCT TCT TTC CCG GCT CCG TCG GCC CGG GGG CCT TGG TCT C-3'(FRAG.NO:1311)(SEQ ID NO:10689)  
 5'-CCT CGT CCT TCB TGG TBC CG-3' (FRAG. NO:1312)(SEQ ID NO:10690)  
 5'-CTCGGTBGB C GCGCTCBB C TCGGGTGGG C CGGTGGTGB G CGGCGGCB C B CGCGBBGG C CCTGCGCGCC GGBGTCBCCTG  
 CBGGGBBGG TBGGCTTGC B GCBGBCTCC CBGGBGGGT BCBGCBGCC B GTBGBGCTBC CTCGCTCTC BTGGTBCCGT  
 CGGTGTGGT G CBCCGGGCTG TGTGTBBGG CGBGCTGG-3' (FRAG.NO:1861) (SEQ ID NO:11243)

#### 10 Human Endothelin-1 Nucleic Acids and Antisense Oligonucleotide Fragments

5'-BCCGGCGGBG CCGCCBGGGT GGBCTGGGG TGGGTTTCTC CCGCCGTT CCBCCCBCCG CGCTGBGCTC BCGCCTBBG  
 BCTGCTGTTT CTGGBGCTCC TTGGCBGGC BCBBCBGB B GBBGBBBBT CBTGBGCB B TBBTCCBTTC TGBBBBBBBG  
 GGBTCBBBBB CCTCCCGTTC CCGTTCGCC TGGCGCGCGC TGCGGGTTCC TCGTGGGTTT CTCCCCCGC TTCTCCGGTC  
 TGTTCCTTT GTGGGCTCT TGTCTTTTG GTCTTCTTT TCCGCTTGG CGTCTTTCC TTCTTTGTG CTCGGTTGTG  
 15 GGTCCGCTGG TCCTTTGCC TGTGTGTTT TGCTGCCCGT TCGCTGGCG CGCGCTGCG GTTCTCTGT GGTTCCTCC  
 CGCCGTCTC CGGTCTGTG CTTTGTGG CTTCTGTCT TTTTGGCTGT TCTTTCTCT CTGGCGTCT TTCTCTTCT  
 TTGTGCTCG TTGTGGTCC GCTGGTCTT TGCCCTGTGT GTTCTGCTG-3' (FRAG. NO:1862) (SEQ ID NO:11244)

5'-CCGGCGGBG CCGCCBGGGT GGBCTGGGG TGGGTTTCTC CCGCCGTT CCBCCCBCCG CGCTGBGCTC BCGCCTBBG

5'-CCGCCBGGG-3' (FRAG. NO:1864) (SEQ ID NO:11246)

5'-GGCGCGCGC-3' (FRAG. NO:1865) (SEQ ID NO:11247)

5'-GTGGGTCCGC-3' (FRAG. NO:1866) (SEQ ID NO:11248)

5'-CCCCTTCGCTGGCGC-3' (FRAG. NO:1313)(SEQ ID NO:10691)

5'-GCGCTGCGGGTTCCTC-3' (FRAG. NO:1314)(SEQ ID NO:10692)

5'-GTGGGTTTCTCCCGCCGTTCTC-3' (FRAG. NO:1315)(SEQ ID NO:10693)

5'-CGGTCTGTGCTTGTGGG-3' (FRAG. NO:1316)(SEQ ID NO:10694)

5'-CTTCTGTCTTTTGGCT-3' (FRAG. NO:1317)(SEQ ID NO:10695)

5'-GTCTTTTCTGCTTGGC-3' (FRAG. NO:1318)(SEQ ID NO:10696)

5'-GTCTTTTCTTCTT-3' (FRAG. NO:1319)(SEQ ID NO:10697)

5'-TGTGCTCGGTTGTGGTC-3' (FRAG. NO:1320)(SEQ ID NO:10698)

5'-CGCTGGTCTTTGCC-3' (FRAG. NO:1321)(SEQ ID NO:10699)

5'-CTGTGTGTTTCTGCTG-3' (FRAG. NO:1322)(SEQ ID NO:10700)

5'-CCCGTTGCGCTGGCGC-3' (FRAG. NO:1323)(SEQ ID NO:10701)

5'-GCGCTGCGGGTTCCTC-3' (FRAG. NO:1324)(SEQ ID NO:10702)

5'-GTGGGTTTCTCCCGCCGTTCTC-3' (FRAG. NO:1325)(SEQ ID NO:10703)

5'-CGGTCTGTGCTTTGTGGG-3' (FRAG. NO:1326)(SEQ ID NO:10704)

5'-CTTCTGTCTTTTGGCT-3' (FRAG. NO:1327)(SEQ ID NO:10705)

5'-GTTCTTTCTGCTTGGC-3' (FRAG. NO:1328)(SEQ ID NO:10706)

5'-GTCTTTTCTTCTT-3' (FRAG. NO:1329)(SEQ ID NO:10707)

5'-TGTGCTCGGTTGTGGTC-3' (FRAG. NO:1330)(SEQ ID NO:10708)

5'-CGCTGGTCTTTGCC-3' (FRAG. NO:1331)(SEQ ID NO:10709)

5'-CTGTGTGTTTCTGCTG-3' (FRAG. NO:1332)(SEQ ID NO:10710)

#### Endothelin Receptor ET-B Nucleic Acids and Antisense Oligonucleotide Fragments

5'-GCCCTGTGG GCGGAAGCC TCTCTCTCT CCCCAGATC CCGACAGGC CGCAGGCAAG AACCAGCGCA ACCAGGGCGC  
 GTCCGCACAG ACTTGGAGGC GGCTGCATGC TGCTACCTGC TCCAGAAGCG TCCGGTGGCC GCCGCGCC CTGTGGGGC  
 45 GBBGCGCTCT CTCCTCTCC CBGCTCCGCG BCBGGCCGB GGBBGBBCC BCGCBBCB GGGCGCGTCC GCBGBCTT  
 GBBGGCGCT GCBTGTGCT BCTGCTCGGG GBBGCGCTCC GTGGCCCGC CGCGTCCGGT GGCCCGCGC CCTCTCTCT  
 CTCCCGTGG CCTGTGGG CGGTCTCTC CGTCTGTCT CTTTCTTT TGTGTCTT TCTCCCGTC TCTGCTT-3' (FRAG.  
 NO: 1867) (SEQ ID NO:11249)

5'-CGGGCG GBBBGC-3' (FRAG. NO: 1868) (SEQ ID NO:11250)

5'-CGGGCGGG-3' (FRAG. NO: 1869) (SEQ ID NO:11251)

5'-CCGCBGBGC-3' (FRAG. NO: 1870) (SEQ ID NO:11252)

5'-GCGTCCGGTGGCCGCGC-3' (FRAG. NO:1333)(SEQ ID NO:10711)

5'-GCCTCTCTCTCTCC-3' (FRAG. NO:1334)(SEQ ID NO:10712)

5'-GTGGCCCTGTGCGGCGG-3' (FRAG. NO:1335)(SEQ ID NO:10713)

5'-TCCTGCCGTCTGTCTCTT-3' (FRAG. NO:1336)(SEQ ID NO:10714)

5'-TCTTTGTGTCTTGT-3' (FRAG. NO:1337)(SEQ ID NO:10715)

5'-CTTCCCGTCTCTGCTT-3' (FRAG. NO:1338)(SEQ ID NO:10716)

5'-GCCCTGTGG GCGGAAGCC TCTCTCTCT CCCCAGATC CCGACAGGC CGCAGGCAAG AACCAGCGCA ACCAGGGCGC  
 GTCCGCACAG ACTTGGAGGC GGCTGCATGC TGCTACCTGC TCCAGAAGCG TCCGGTGGCC GCCGCGC-3' (FRAG. NO: 1871) (SEQ  
 ID NO:11253)

5'-GCCCTGTGG GCGGGBGCC TCTCTCTCT CCCCGBTCC GCBGBGCC GCBGGCBGB BCCBGCGB BCCBGGCGC  
 GTCCGCBGB BCTTGGGGC GGCTGCTGC TGCTBCTGC TCCBGBGCC TCCGGTGGCC GCCGCGC-3' (FRAG. NO: 1872) (SEQ  
 ID NO:11254)

#### Endothelin ETA Receptor Nucleic Acids and Antisense Oligonucleotide Fragments

5'-GTCTGTCTC CCGTCTCTT CCACTGCTT CTCCCGGGG CTTCGCCGC TCGGGTGGC CGGTGTCCG GGCTCCGGC  
 CGGCGCGGC TTCGGTGGC GGTGGTGGC GCGGCTGCC GGTCCGCGC GCGCCTGGC CCTTGTGCT GTTTTGTCT  
 TGTTCGTTT TGGTGTCTT GGTCTGTGT GTGTGTGTT GTTTCTTCT TGGGTGTGG CCTTGGGTT TTGGTGTGG  
 GCCCTTTGG GCCTTGGCT CTGGCTGCT TGTCTCCC GTCTCTCCC ACTGCTTCT CCGGGGGCT TCCCGGCTT  
 CGGTGGCGC GTGTCCGG CTCCGGCGC GCGCGGCT CGGTGCGG TGGGTGGCG GGGCTGCCG GTCCGCGCG  
 70 CGCTGGGCC CTGTGCTGC TTTTGTCTT TTCCGTTCT GCTGCTCCG TCTGTGTGT GGTGTGTTT TTTTCTTCT  
 GGTGTGGGC TTGGGTTT GGCTGTGGC CCTTGGGGC CTGGCTTCT GGCTCCAT CCACATGATT GCTTAGATT  
 GTGCTGTATC TCTCAGGATT ATCACTGATT ACACATCAA CAGTGCCAG CAAAAGGAT GCCCTGAGG AAAGGGTTT  
 CATCTTGAG CAAATTGAG GACBTCCB BTGTTGCTT BGTTTGTGC TGTBTCTCT BGGTTTCTB CTGTTTCTB



BTCCBBCCBG TGCCBGCCBB BBGGBTGCCC TGBGGCBBBG GGTTCBCBTC TTGBGGCBBB TTTGBGGB-3' (FRAG. NO:1873)  
(SEQ ID NO:11255)  
5'-GBGGCBBBGGG-3' (FRAG. NO:1874) (SEQ ID NO:11256)  
5'-GCCBGCCBB BBGGB-3' (FRAG. NO:1875) (SEQ ID NO:11257)  
5'-CGCCTGGGCC C-3' (FRAG. NO:1876) (SEQ ID NO:11258)  
5'-GTCTGTCTCCCGTCTCCTCC-3' (FRAG. NO:1339)(SEQ ID NO:10717)  
5'-ACTGCTTCTCCCGGGG-3' (FRAG. NO:1340)(SEQ ID NO:10718)  
5'-GCTTCCCGGGCTTC-3' (FRAG. NO:1341)(SEQ ID NO:10719)  
5'-GGGTGGCCGGTGTCCCGGGTCCGGCGCGGCGGC-3' (FRAG. NO:1342)(SEQ ID NO:10720)  
5'-GGCTTCGGCTGC-3' (FRAG. NO:1343)(SEQ ID NO:10721)  
5'-GGGTGGGTGGCGCGG-3' (FRAG. NO:1344)(SEQ ID NO:10722)  
5'-GCTGCCGGGTCCCGCGCGGCGCTGGGCC-3' (FRAG. NO:1345)(SEQ ID NO:10723)  
5'-CTTGTGCTGCTTTT-3' (FRAG. NO:1346)(SEQ ID NO:10724)  
5'-TGCTTGTTCGTTTC-3' (FRAG. NO:1347)(SEQ ID NO:10725)  
5'-TGGCTGCTCCGGTCTGTGTTGTGGTTGTTT-3' (FRAG. NO:1348)(SEQ ID NO:10726)  
5'-TTTCTTCTTGGGTGTGGG-3' (FRAG. NO:1349)(SEQ ID NO:10727)  
5'-CCTTGGCGTTTGG-3' (FRAG. NO:1350)(SEQ ID NO:10728)  
5'-CTGTGGGCCCTTTG-3' (FRAG. NO:1351)(SEQ ID NO:10729)  
5'-GGGCCCTTGGCTTCTGGGCTC-3' (FRAG. NO:1352)(SEQ ID NO:10730)  
5'-CATCCACATG ATTGCTTAGA TTTGTGCTGT ATCTCTCAGG ATTACACATC CAACCAAGTGC CAGCCAAAAG  
GATGCCCTGA GGCAGAGGGT TTCCATCTTG AGGCAAAATT GAGGA-3' (FRAG. NO:1353) (SEQ ID NO:10731)  
5'-CBTCCBCBTG BTTGCTTBGB TTTGTGCTGT BTCTCTCBGG BTTBTCBTC CBBCCBGTCG CBGCCBBBGG  
GBTGCCCTGB GGCBBBGGGT TTCCBTCTTG BGGCBBBTTT GBGGB-3' (FRAG. NO:1354)(SEQ ID NO:10732)  
Endothelin Receptor A Nucleic Acid and Antisense Oligonucleotide Fragments  
25 5'-GCCACCATGG AAACCCCTTTC CCTCAGGGCA TCCTTTTGGC TGGCACTGGT TGGATGTGTA ATCAGTGATA ATCCTGAGAG  
ATACAGCACA AATCTAAGCA ATCATGTGGA TGATTTCACC ACITTTTCGTG GCACAGAGCT CAGCTTCCTG GTTACCACCTC  
ATCAACCCAC TAATTTGGTC CTACCCAGCA ATGGCTCAAT GCACAACTAT TGCCACAGC AGACTAAAAAT TACTTCAGCT  
TTCAAATACA TTAACACTGT GATATCTGT ACTATTTTCA TCGTGGGAAT GGTGGGGAAT GCAACTCTGC TCAGGATCAT  
TTACCAGAAC AAATGTATGA GGAATGGCCC CAACGCGCTG ATAGCCAGTC TTGCCCTTGG AGACCTTATC TATGTGTTCA  
30 TTGATCTCCC TATCAATGTA TGGCTGGGCG CTGGCCTTTT GATCACAATG ACTTTGGCGT ATTTCTTTGC AAGCTGTTC  
CCTTTTGGCA GAAGTCTCTG GTGGGGATCA CCGTCTCAA CCTCTGCGCT CTTAGTGTG ACAGGTACAG AGCAGTTGCC  
TCCTGGAGTC GTTTCAGGG AATTGGGATT CTCTGGTAA CTGCCATTGA AATTGCCTCC ATCTGGATCC TGTCTTTAT  
CCTGGCCATT CCTGAAGCGA TTGGCTTCGT CATGGTACCC TTGAATATA GGGGTGGACA GCATAAAACC TGTATGCTCA  
ATGCCACATG AAAATTCATG GAGTTCATCC AAGATGTAAA GGAATGGTGG CTCTTCGGGT TCTATTTCTG TATGCCCTTG  
35 GTGTGCATCG CGATCTCTA CACCCTCATG ACTGGTGAGA TGTGAAACAG AAGGAATGGC AGCTTGAGAA TTGCCCTCAG  
TGAACATCTT AAGCAGCGTC GAGAAGTGGC AAAAACAGTT TTCTGCTTGG TTGTAATTTT TGCTCTTTGC TGGTTCCTC  
TTCAATTAAG CCGTATATTG AAGAAAACCTG TGTATAACGA GATGGACAAG AACCGATGTG AATTACTTAG TTCTTACTG  
CTCATGGATT ACATCGGTAT TAACCTGGCA ACCATGAATT CATGTATAAA CCCCATAGCT CTGTATTTTG TGAGCAAGAA  
ATTTAAAAAT TGTTTCCAGT CATGCCCTCG CTGCTGCTGT TACCAGTCCA AAAGTCTGAT GACCTCGGTG TTGCCCTCAG  
40 GAACAAGCAT CCAAGTGAAG AACACGATC AAAACAACCA CAACACAGAC CGGAGCAGCC ATAAGGACAG CATGAACCTGA  
CCACCCTTAG AAGCACTCCT GAATTCGGGA AAAAGTGAAG GTGTAAAAGC AGCACAAGTG CAATAAGAGA TATTTCTCA  
AATTTGCCTC AAGATGGAAG CCCTTTCCT CAGGGATCCT TTTTGGTGG CACTGGTTGG ATGTGTAATC AGTGATAATC  
CTGAGAGATA CAGCACAATC CTAAGCAATC ATGTGGATGA TTTCACCACT TTTCGTTGGA CAGAGCTCAG CTTCCTGGTT  
ACCACTCATC AACCCACTAA TTTGGTCTA CCCAGCAATG GCTCAATGCA CAACTATTGC CCACAGCAGA CTAATAATTAC  
45 TTCAGCTTTC AAATACATTA AACTGTGAT ATCTTGTAAT ATTTTCATCG TGGGAATGGT GGGGAATGCA ACTCTGCTCA  
GGATCAATTA CCAGAACAAA TGTATGAGGA ATGGCCCAA CGCGCTGATA GCCAGTCTTG CCTTGGAGA CCTATCTAT  
GTGGTCATTG ATCTCCCTAT CAATGTATTT AAGCTGCTGG CTGGGCGCTG GCCTTTTGAT CACAATGACT TTGGCGTATT  
TCTTTGCAAG CTGTTCCCTT TTTTGCAAGG GTCCCTCGTG GGGATCACCG TCCTCAACCT CTGCGCTCTT AGTGTGACA  
GGTACAGAGC AGTTGCTCTC TGGAGTCTGT TTCAGGGAAT TGGGATTCCT TTGGTAACTG CCATTGAAAT GTCTCTCATC  
50 TGGATCCTGT CCTTATCCT GGCCATTCCT GAAGCGATTG GCTTCGTCAT GGTACCCCTT GAATATAGGG GTGAACAGCA  
TAAAACCTGT ATGCTCAATG CCACATCAA ATTCAATGAG TTCTACCAAG ATGTAAAGGA CTGGTGCTC TTCGGGTCT  
ATTCTGTAT GCCCTTGGTG TGCATGCGA TCTTCTACAC CCTCATGACT TGTGAGATGT TGAACAGAAG GAATGGCAGC  
TTGAGAAATT GCCCTAGTGA ACATCTTAAG CAGCTGCGAG AAGTGGCAAA AACAGTTTTC TGCTTGTTG TAATTTTTC  
TCTTTGCTGG TTCCCTCTTC ATTTAAGCCG TATATTGAAG AAAACTGTGT ATAACGAGAT GGACAAGAAC CGATGTGAAT  
55 TACTTAGTTT CTTACTGCTC ATGGATTACA TCGGTATTAA CTGGGCAACC ATGAATTCAT GTATAAACCC CATAGCTCTG  
TATTTTGTGA GCAAGAAAT TAAAAATTTG TTCCAGTATC GCCTCTGCTG CTGCTGTTAC CAGTCCAAA GTCTGATGAC  
CTCGTCCCC ATGAACCGAA CAAGCATCCA GTGGAAGAAC CACGATCAAA ACAACCAAA CACAGACCGG AGCAGCCATA  
AGGACAGCAT GAACTGACCA CCCTAGAAG CACTCCTCGG TACTCCATA ATCCTCTCGG AGAAAAAAT CACAAGGCAA  
CTGTGAGTCC GGGAAATCTCT TCTGTATCC TCTTCTCTA ATCACTCCC ACACCAAGA AGAAATGCTT TCCAAAACCG  
60 CAAGGGTAGA CTGTTTTATC CACCCACAAC ATCTACGAAT CGTACTCTT TAATTGATCT AATTTACATA TTCTGCGTGT  
TGTATTACAG ACTAAAAAAT GGTGGGAGCT GGGGAGAAAT GAAGACTGTT AAATGAAACC AGAAGGATAT TTAATCTTT  
TGCATGAAAA TAGAGCTTTC AAGTACATGG CTAGCTTTTA TGGCAGTTCT GGTGAATGTT CAATGGGAAC TGGTCAACAT  
GAAACTTTAG AGATTAACGA CAAGATTTTC TACTTTTTT AAGTGATTTT TTTGCTCTC AGCCAAACAC AATATGGGT  
CAAGTCACTT TTATTTGAAA TGTCAATTTG TGTCAATTTT CCGAATTC GAATTCGGGA AAAAGTGAAG GTGTAAAAGC  
65 AGCACAAGTG CAATAAGAGA TATTTCTCA AATTTGCCTC AAGATGGAAG CCCTTTCCTC CAGGGCATCC TTTTGGCTGG  
CACTGGTTGG ATGTGTAATC AGTGATAATC CTGAGAGATA CAGCAAAAT CTAAGCAATC ATGTGGATGA TTCAACCAT  
TTTCGTGGCA CAGAGCTCAG CTTCCTGGTT ACCACTATC AACCCACTAA TTTGGTCTA CCCAGCAAT CCCAATGCA  
CAACTATTGC CCACAGCAGA CTAATAATTAC TTACGCTTTC AAATACATTA AACTGTGAT ATCTTGTAAT ATTTTCATCG  
TGGGAATGGT GGGGAATGCA ACTCTGCTCA GGTATCAATTA CCAGAACAAA TGTATGAGGA ATGGCCCAA CGCGCTGATA  
70 GCCAGTCTTG CCCTTGGAGA CCTTATCTAT GTGGTCAATT ATCTCCCTAT CAATGTATTT AAGCTGCTGG CTGGGCGCTG  
GCCCTTTTGT CACAATGACT TTGGCGTATT TCTTTGCAAG CTGTTCCCTT TTTTGCAGAA GTCCTCGGTG GTGCAATCCG  
TCCTCAACCT CTGCGCTCTT AGTGTGACA GGTACAGAGC AGTTGCCTCC TGGAGTCTG TTCAGGGAAT TGGGATTCCT  
TTGGTAACTG CCATTGAAAT TGTCTCCATC TGGATCCTGT CCTTTATCCT GGCCATTCCT GAAGCGATTG GCTTCGTAT  
GGTACCCTTT GAATATAGGG GTGAACAGCA TAAACCTGT ATGCTCAATG CCACATCAA ATTCATGAG TTCTACCAAG  
75 ATGTAAAGGA CTGGTGCTC TTCGGGTCTT ATTCTGTAT GCCTTGGTG TGCATGCGA TCTTCTACAC CCTCATGACT

TGTGAGATGT TGAACAGAAG GAATGGCAGC TTGAGAAATG CCCTCAGTGA ACATCTTAAG CAGCGTCGAG AAGTGGCAAA  
 AACAGTTTTT TGCTTGGTTG TAATTTTTCG TCTTTGCTGG TTCCCTCTTC ATTTAAGCCG TATATTGAAG AAAACTGTGT  
 ATAACGAGAT GGACAAGAAG CGATGTGAAT TACTTAGTTT CTCTAGCTCT ATGGATTACA TCGGTATTAA CTGGCAACC  
 ATGAATTCAT GTATAAACC CATAGCTCTG TATTTTGTGA GCAAGAAATT TAAAAATTGT TTCCAGTCAT GCCTCTGCTG  
 5 CTGCTGTTAC CAGTCCAAAA GTCTGATGAC CTCGGTCCCC ATGAACGGAA CAAGCATCCA GTGGAAGAAC CACGATCAAA  
 ACAACCACAA CACAGACCGG AGCAGCCATA AGGACAGCAT GAATGACCA CCCTTAGAAG CACTCCTCGG TACTCCATA  
 ATCCTCTCGG AGAAAAAAT CACAAGGCAA CTGTGAGTCC GGGAAATCTCT TCTCTGATCC TTCTTCTTIA ATTACTCCC  
 ACACCCAAGA AGAAATGCTT TCCAAAACCG CAAGGGTAGA CTGGTTTATC CACCCACAAC ATCTACGAAT CGTACTTCTT  
 TAATTGATCT AATTACATA TTCTGCGTGT TGTATTGAGC ACTAAAAAT GGTGGGAGCT GGGGGAAGT GAAGACTGTT  
 10 AAAAGAAAAC AGAAGGATAT TTACTACTTT TGCATGAAAA TAGAGCTTTT AAGTACATGG CTAGCTTTTA TGGCAGTCT  
 GGTGAATGTT CAATGGGAAC TGGTCACCAT GAAACTTTAG AGATTAACGA CAAGATTTTC TACTTTTTTT AAGTGATTTT  
 TTTGCTCTC AGCCAAACAC AATATGGGCT CAAGTCACIT TTATTGAAA TGTCATTGG TGCCAGTATC CCGAATTC-3' (FRAG.  
 NO: ) (SEQ ID NO:12383)  
 5'-GAATTCGGGA AAAAGTGAAG GTGTAAAAGC AGCACAAGTG CAATAAGAGA TATTTCTCA AATTGCGCTC AAGATGGAAA  
 15 CCCTTTGCTT CAGGGCATCC TTTTGCTGG CACTGGTTGG ATGTGTAATC AGTGATAATC CTGAGAGATA CAGCACAAAT  
 CTAAGCAATC ATGTGGATGA TTTCACCACT TTTCGTGGCA CAGAGCTCAG CTTCCTGGTT ACCACTCATC AACCCACTAA  
 TTTGGTCTTA CCCAGCAATG GCTCAATGCA CAACTATTGC CCACAGCAGA CTAATAATTAC TTCAGCTTTC AAATACATTA  
 ACACGTGAT ATCTTGTACT ATTTTCATCG TGGGAATGGT GGGGAATGCA ACTCTGCTCA GGATCATTTA CCAGAACAAA  
 TGTATGAGGA ATGGCCCCAA CGCGCTGATA GCCAGTCTTG CCCTTGGAGA CCTTATCTAT GTGGTCATTG ATCTCCCTAT  
 20 CAATGTATTT AAGCTGCTGG CTGGGCGCTG GCCTTTTGAT CACAATGACT TTGGCGTATT TCTTTGCAAG CTGTTCCCTC  
 TTTTGAGAAA GTCCTCGGTG GGGATCACCG TCCTCAACCT CTGCGTCTT AGTGTGACA GGTACAGAGC AATTGCTCTC  
 TGGAGTCGTG TTCAGGGAAT TGGGATTCCT TTGGTAACCT CCATTGAAAT TGTCTCCATC TGGATCCTGT CCTTATCCT  
 GGCCATTCTT GAAGCGATG GCTTCGTCAT GGTACCCCTT GAATATAGGG GTGAACAGCA TAAAACCTGT ATGCTCAATG  
 CCACATCAAA ATTCATGGAG TTCTACCAAG ATGTAAAGGA CTGGTGGCTC TTCGGGTCTT ATTTCTGTAT GCCCTGGTG  
 25 TGCATTCGCA TCTTCTACAC CCTCATGACT TGTGAGATGT TGAACAGAAG GAATGGCAGC TTGAGAATTG CCCTCAGTGA  
 ACATCTTAAG CAGCGTCGAG AAGTGGCAAA AACAGTTTTT TGCTTGGTTG TAATTTTTCG TCTTTGCTGG TTCCCTCTTC  
 ATTTAAGCCG TATATTGAAG AAAACTGTGT ATAACGAGAT GGACAAGAAC CGATGTGAAT TACTTAGTTT CTACTGCTC  
 ATGGATTACA TCGGTATTAA CTGGCAACC CTGTGAAATC GTATAAACCC CATAGCTCTG TATTTTGTGA GCAAGAAATT  
 TAAAAATTGT TTCCAGTCAT GCCTCTGCTG CTGCTGTTAC CAGTCCAAAA GTCTGATGAC CTCGGTCCCC ATGAACGGAA  
 30 CAAGCATCCA GTGGAAGAAC CACGATCAAA ACAACCACAA CACAGACCGG AGCAGCCATA AGGACAGCAT GAACTGACCA  
 CCCTTAGAAG CACTCCTCGG TACTCCATA ATCCTCTCGG AGAAAAAAT CACAAGGCAA CTGTGAGTCC GGGAAATCTCT  
 TCTCTGATCC TTCTTCTTA ATTCACTCCC ACACCCAAGA AGAAATGCTT TCCAAAACCG CAAGGGTAGA CTGGTTTATC  
 CACCCACAAC ATCTACGAAT CGTACTTCTT TAATTGATCT AATTACATA TTCTGCGTGT TGTATTGAGC ACTAAAAAT  
 GGTGGGAGCT GGGGGAAGT GAAGACTGTT AAATGAAACC AGAAGGATAT TTACTACTTT TGCATGAAAA TAGAGCTTTT  
 35 AAGTACATGG CTAGCTTTTA TGGCAGTCTT GGTGAATGTT CAATGGGAAC TGGTCACCAT GAAACTTTAG AGATTAACGA  
 CAAGATTTTC TACTTTTTTT AAGTGATTTT TTTGCTCTC AGCCAAACAC AATATGGGCT CAAGTCACIT TTATTGAAA  
 TGTCATTGG TGCCAGTATC CCGAATTC-3' (FRAG. NO: ) (SEQ ID NO:11851)  
 5'-GAATTCGGGA AAAAGTGAAG GTGTAAAAGC AGCACAAGTG CAATAAGAGA TATTTCTCA AATTGCGCTC AAGATGGAAA  
 40 CCCTTTGCTT CAGGGCATCC TTTTGCTGG CACTGGTTGG ATGTGTAATC AGTGATAATC CTGAGAGATA CAGCACAAAT  
 CTAAGCAATC ATGTGGATGA TTTCACCACT TTTCGTGGCA CAGAGCTCAG CTTCCTGGTT ACCACTCATC AACCCACTAA  
 TTTGGTCTTA CCCAGCAATG GCTCAATGCA CAACTATTGC CCACAGCAGA CTAATAATTAC TTCAGCTTTC AAATACATTA  
 ACACGTGAT ATCTTGTACT ATTTTCATCG TGGGAATGGT GGGGAATGCA ACTCTGCTCA GGATCATTTA CCAGAACAAA  
 TGTATGAGGA ATGGCCCCAA CGCGCTGATA GCCAGTCTTG CCCTTGGAGA CCTTATCTAT GTGGTCATTG ATCTCCCTAT  
 45 CAATGTATTT AAGCTGCTGG CTGGGCGCTG GCCTTTTGAT CACAATGACT TTGGCGTATT TCTTTGCAAG CTGTTCCCTC  
 TTTTGAGAAA GTCCTCGGTG GGGATCACCG TCCTCAACCT CTGCGTCTT AGTGTGACA GGTACAGAGC AATTGCTCTC  
 TGGAGTCGTG TCGAGGGAAT TGGGATTCCT TTGGTAACCT CTAAGTGAAT TGTCTCCATC TGGATCCTGT CCTTATCCT  
 GGCCATTCTT GAAGCGATG GCTTCGTCAT GGTACCCCTT GAATATAGGG GTGAACAGCA TAAAACCTGT ATGCTCAATG  
 CCACATCAAA ATTCATGGAG TTCTACCAAG ATGTAAAGGA CTGGTGGCTC TTCGGGTCTT ATTTCTGTAT GCCCTGGTG  
 50 TGCATTCGCA TCTTCTACAC CCTCATGACT TGTGAGATGT TGAACAGAAG GAATGGCAGC TTGAGAATTG CCCTCAGTGA  
 ACATCTTAAG CAGCTGAGG AAGTGGCAAA AACAGTTTTT TGCTTGGTTG TAATTTTTCG TCTTTGCTGG TTCCCTCTTC  
 ATTTAAGCCG TATATTGAAG AAAACTGTGT ATAACGAGAT GGACAAGAAC CGATGTGAAT TACTTAGTTT CTACTGCTC  
 ATGGATTACA TCGGTATTAA CTGGCAACC ATGAATTCAT GTATAAACCC CATAGCTCTG TATTTTGTGA GCAAGAAATT  
 TAAAAATTGT TCCAGTCAT GCCTCTGCTG CTGCTGTTAC CAGTCCAAAA GTCTGATGAC CTCGGTCCCC ATGAACGGAA  
 55 CAAGCATCCA GTGGAAGAAC CACGATCAAA ACAACCACAA CACAGACCGG AGCAGCCATA AGGACAGCAT GAACTGACCA  
 CCCTTAGAAG CACTCCTCGG TACTCCATA ATCCTCTCGG AGAAAAAAT CACAAGGCAA CTGTGAGTCC GGGAAATCTCT  
 TCTCTGATCC TTCTTCTTA ATTCACTCCC ACACCCAAGA AGAAATGCTT TCCAAAACCG CAAGGGTAGA CTGGTTTATC  
 CACCCACAAC ATCTACGAAT CGTACTTCTT TAATTGATCT AATTACATA TTCTGCGTGT TGTATTGAGC ACTAAAAAT  
 GGTGGGAGCT GGGGGAAGT GAAGACTGTT AAATGAAACC AGAAGGATAT TTACTACTTT TGCATGAAAA TAGAGCTTTT  
 AAGTACATGG CTAGCTTTTA TGGCAGTCTT GGTGAATGTT CAATGGGAAC TGGTCACCAT GAAACTTTAG AGATTAACGA  
 60 CAAGATTTTC TACTTTTTTT AAGTGATTTT TTTGCTCTC AGCCAAACAC AATATGGGCT CAAGTCACIT TTATTGAAA  
 TGTCATTGG TGCCAGTATC CCGAATTC-3' (FRAG. NO: ) (SEQ ID NO:11839)  
 5'-GCCACCATGG AAACCTTTG CCTCAGGGA TCCTTTTGGC TGGCACTGGT TGGATGTGTA ATCAGTGATA ATCTGAGAG  
 ATACAGCACA AATCTAAGCA ATCATGTGGA TGAATTCACC ACTTTTCGTG GCACAGAGCT CAGCTTCTGT GTTACCACCT  
 65 ATCAACCCAC TAATTTGGTC CTACCCAGCA ATGGCTCAAT GACACAATC TGCCACAGC AGACTAAAAAT TACTTCAGCT  
 TTCAAATACA TTAACACTGT GATATCTTGT ACTATTTTCA TCGTGGGAAT GGTGGGGAAT GCAACTCTGC TCAGGATCAT  
 TTACCAAGAA AAATGATGTA GGAATGGCCC CAACGGCTG ATAGCCAGTC TTGCCCTTGG AGACCTTATC TATGTGGTCA  
 TTGATCTCCC TATCAATGTA TGGCTGGGCG CTGGCTCTTA GATCACAATG ACTTTGGCGT ATTTCTTTCG AATGTTTCC  
 CCTTTTTCGA GAAGTCCTCG CTGCTGATCA CCGTCTTAAA CCTCTGCGCT CTAGTGTG ACAGGTACAG AGCAGTTGCC  
 TCCTGGAGTC GTGTTACGGG AATTGGGATT CCTTTGGTAA CTGCCATTGA AATTGCTCTC ATCTGGATCC TGTCTTTAT  
 70 CCTGGCCATT CCTGAAGCGA TTGGCTTCGT CATGGTACCC TTGGAATATA GGGGTGGACA GCATAAAACC TGTATGCTCA  
 ATGCCACATA AAAATTCATG AAGTTCTACC AAGATGTAAA GGCATGGTGG CTCTTCGGGT TCTATTCTGT TATGCCCTTG  
 GTGTGCACTG CGATCTTCTA CACCCTCATG ACTGGTGAGA TGTGAACAG AAGGAATGGC AGCTTGAGAA TTGCCCTCAG  
 TGAACATCTT AAGCAGCGTC GAGAAGTGGC AAAAACAGTT TTCTGCTTGG TTGTAATTTT TGCTCTTTCG TGGTTCCCTC  
 TTCATTAAAG CCGTATATTG AAGAAAACTG TGTATAACGA GATGGACAAG AACCGATGTG AATTACTTAG TTCTTACTG  
 75 CTCATGGATT ACATCGGTAT TAACCTGGCA ACCATGAATT CATGTATAAA CCCCATAGCT CTGTATTTCG TGACCAAGAA

ATTTAAAAAT TGTTTCCAGT CATGCCTCTG CTGCTGCTGT TACCAGTCCA AAAGTCTGAT GACCTCGGTC CCCATGAACG  
GAACAAGCAT CCAGTGGAA G AACCACGATC AAAACAACCA CAACACAGAC CGGAGCAGCC ATAAGGACAG CATGAAGTGA  
CCACCCTTAG AAGCACTCCT-3' (FRAG. NO: ) (SEQ ID NO:12486)

**Substance P Antisense Nucleic Acids and Oligonucleotide Antisense Oligonucleotide Fragments**

5 5'-CTGCTGBGGC TTGGGTCTCC GGGCGBTCT CTGCBGBBGB TGCTCBBBGG GCTCCGGCBG TTCCTCCTTG BTCTGGTCGCT  
GTCGTBCCBG TCGGBCCBG BTTCBGBTC BTCTTTGGCT CCTTTTCTT CTGCBBBCBG CTGBGTGGBG BCBBGBBBBB  
BGBCTGCCBB GGCCBCBGG BTTCBTGT TGGTTTTCG GBCGBCBGT CCCGCGGGT GCTGAGTTTC TCTGGTCTCT  
CCGBGCCBC GTGGTCGCTC CGCGTTTCT TGGTTCCTCC GGTCCGCGG GGTGCTGTCT GGTGCTGTC GTGGCTGGG  
TCTCCGGCG GTTCTCTCC TTTCCGC-3' (FRAG. NO:1877) (SEQ ID NO:11259)

10 5'-CTCC GGGCB-3' (FRAG. NO:1878) (SEQ ID NO:11260)

5'-GGCCBCBGG-3' (FRAG. NO:1879) (SEQ ID NO:11261)

5'-GGTCTCCGGGCG-3' (FRAG. NO:1880) (SEQ ID NO:11262)

5'-GGG TCTCCGGGCG G-3' (FRAG. NO:1881) (SEQ ID NO:11263)

5'-CGTGGTCGCTCCGC-3' (FRAG. NO:1355)(SEQ ID NO:10733)

15 5'-GTTTCTCTGGTTCCTCCG-3' (FRAG. NO:1356)(SEQ ID NO:10734)

5'-GTCCCGCGGGGTGCTG-3' (FRAG. NO:1357)(SEQ ID NO:10735)

5'-TCTGGTCGCTGCTG-3' (FRAG. NO:1358)(SEQ ID NO:10736)

5'-GGCTTGGTCTCCGGGCG-3' (FRAG. NO:1359)(SEQ ID NO:10737)

5'-GTTTCTCTCTTTCCGC-3' (FRAG. NO:1360)(SEQ ID NO:10738)

20 5'-CTGCTGBGGC TTGGGTCTCC GGGCGBTCT CTGCBGBBGB TGCTCBBBGG GCTCCGGCBG TTCCTCCTTG BTCTGGTCGCT  
GTCGTBCCBG TCGGBCCBG BTTCBGBTC BTCTTTGGCT CCTTTTCTT CTGCBBBCBG CTGBGTGGBG BCBBGBBBBB  
BGBCTGCCBB GGCCBCBGG BTTCBTGT TGGTTTTCG GBCGBCBGT CCCGCGGGT GCTGAGTTTC TCTGGTCTCT  
CCGBGCCBC-3' (FRAG. NO:1882) (SEQ ID NO:11264)

**Substance P Receptor Nucleic Acids and Antisense Oligonucleotide Fragments**

25 5'-GGGCTBBGBT GTCCBCBCT BCTBCCBCGT TGCCBCBCB BGGGTBCC BCBBTGBCCG TGTBGGCBGC TGCCBBBGG  
BCBBTTTGCC BGGCTGGTTG CBCGBBCTGB TTGGTTCCG BGGTGTBTG GGBGTGTTT GGGGBBGGT CTGBGTCCBC  
CGGBBGBBGC TTBTCBTTT CGBBGTBGG CGGTBBBGC CTBCTBCTG TBCBCCBCC CCTCTGCBG CBGBGTCTG  
TCGTGGCGCC TGGGGCTCBG GTCCGGGC TAAGATGATC CACATCTA CCACGTTGCC CACCACAGG GTCCACAA  
TGACCGTGA GGCAGCTGCC CAAAGGACAA TTTGCAGGC TGGTTGCACG AACTGATTG GTTCCGAGG GTTAGTGAG  
30 ATGTTTGGG AGAGGTCTGA GTCCACGGG AGGACGTTAT CCATTTCGAA GCTAGGCGGT AAAGCCCTAC TATCTGTACA  
CAACCCCTCT CTGCAGCAGA GTCTGTCTG GGCCTCTGG GCTCAGGGTC CGTCTGTCTG TGCGCGCTG GGTCTCTCT  
TTGTTGGGCTC TTTGGTGGCT GTGGCTGTG TCTCTGTGT TGTGCGCTG GGTCTGGGG TGTGGCCTT GGGCGTCTC  
CTGGCTCTC CTGCTGGGCC CCC-3' (FRAG. NO:1883) (SEQ ID NO:11265)

5'-GGGBGGBCG-3' (FRAG. NO:1884) (SEQ ID NO:11266)

35 5'-GGGTC CG-3' (FRAG. NO:1885) (SEQ ID NO:11267)

5'-GGGCC CCC-3' (FRAG. NO:1886) (SEQ ID NO:11268)

5'-GTCTGTCTGCTGGCGCTGGGCTC-3' (FRAG. NO:1361)(SEQ ID NO:10739)

5'-TCTTTTGTGGCT-3' (FRAG. NO:1362)(SEQ ID NO:10740)

5'-CTTTGGTGGCTGTGGCTG-3' (FRAG. NO:1363)(SEQ ID NO:10741)

40 5'-TGGTCTCTGTGGTTG-3' (FRAG. NO:1364)(SEQ ID NO:10742)

5'-CTGCCCTGGGTCTGG-3' (FRAG. NO:1365)(SEQ ID NO:10743)

5'-GGGTGTGGCTTGGGGCCGTCTCTGGCTCTCTCTGTTGGCCCC (FRAG. NO:1366)(SEQ ID NO:10744)

5'-GGGCTAAGT GATCCATC ACTACCAGT TGCCACACC AGAGGTCAAC ACAATGACCG TGAGGCAGC TGCCCAAAGG  
ACAATTGGC AGGCTGGTTG CACGAAGTGA TTGGTTCCG AGGTGTTAGT GGAGATGTTT GGGGAGAGGT CTGAGTCCAC  
45 CGGGAGGACG TTATCCATTTC GAAGTAGGC GGTAAAGCCC TACTATCTGTA CACAACCCCT CTCTGCAGCA GAGTCTCTG  
GTGGCGCTG GGGCTCAGGTCC-3' (FRAG. NO:1367)(SEQ ID NO:10745)

5'-GGGCTBBGBT GTCCBCBCT BCTBCCBCGT TGCCBCBCB BGGGTBCC BCBBTGBCCG TGTBGGCBGC TGCCBBBGG  
BCBBTTTGCC BGGCTGGTTG CBCGBBCTGB TTGGTTCCG BGGTGTBTG GGBGTGTTT GGGGBBGGTCT TGBGTCCBC  
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50 GTGGCGCTG GGGCTCBGG TCC-3' (FRAG. NO:1368) (SEQ ID NO:10746)

**Chymase Antisense Nucleic Acids and Oligonucleotides Antisense Oligonucleotide Fragments**

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 20 CCAGAGCTGA AGCTGGTGAG TATCAGGGTT TCTCCCTCTG AAATCTGCAG TATCAGCTCC TGAAACAAAG ATGTTTAGTC  
 TGAAATAGCT GACTCTCTAA CAGGGTTCCA AGATCTCTCT TCAAGAGTCC CACAGAGGAA ATTTCCACTT GGGATGTGTG  
 CCACCCACC CCCACCCCA CCACTGCCA TTCTCTACAG CTTAGGACAC CCCCAGGAAC AAGGAATTTC ACCTCAATTG  
 TAGAAAAAGCC CAGAGCAAGT GGAAGGAAAA GGGGTATCCC CAGGAAAAACA GACATGTCTT CTTAATCTTC TGAGCATCAG  
 GGCTACCAT TACTTTGTA CTTTCTCACT CTGTGACCAT GCTCAAGAGC TATGGAGAAA TCTAAAAAG GAACCTGGAC  
 25 AGTGGGTCTT ACACAGAGAC AGAGGAGAGT GGGCCAGGGC AAGGTGGGAG TGGGAGAAAT CTGAGATGAA AACATCAGAA  
 TGGAGCAGAG GCAAGAATGA GATTTCACCT GGGAGGTTAT GGGTGGGGAA AGATACGAAA TACAGGAGAC AGGAGAGGGA  
 AGATGGGCGG AACACAGGGT GAGAATGAGA TTCCAGGGAA GCCTAGCTCA GCTTTAACC AATTGTCCA TTCATTGGAG  
 AGAGTATCTA TGGCCGTGTT CAAACCTGG GGTGCTCTGT TCCAGGGGAG ATCATCGGGG GCACAGAAATG GAACCCACAT  
 TCCCGCCCTT ACATGGCCTA CTTGGAATTT GTAACCTCCA ACGTCCCTC AAAATTTTGT GGTGGTTTCC TTATAAGACG  
 30 GAACCTTTGTG CTGACGGCTG CTCAATTGTC AGGAAGGTGA GACAACAGGG TCTATTTATC TCCAAATGGG AGATGAACAA  
 CCAGAGTAGC ATCCAGGAAT ACACCTGCAC TGGGAGCTGA AGAGGGGGTC CTGGGTCTTG TCAACTTTCA GGAGAGGGAA  
 GACTTTGGG TGAAAGACTT TAGTCTGTG TTGAATAGTT CCTTGAGCCT CAGTCACTGA GCTAAGCTCC CTTCCGAGGA  
 AAAGGAGGTC CTGTCCGAAG GTCCCTCTTG TTGAGTAGC ACCCTCACC CCTACCCAAC TCAAGACACA CGGCTCACTT  
 TTCAGGGCCC CACCCAGTCT CAGGGCCACT TCCTCTATGG CCTTTTCAAG AACACTGGCT CTAGTTCTCA GGGTCTGAA  
 35 CCAATCATTT TATGGGAGCA GAGAACAGGT CTACATAAGA CCCCACCTTT CCGTTTAA GCTGATCTCT CTTGCTCAGG  
 GGCTGGCCCT CATGCAGGGT TCCCTGAATT AGGAAGTGTG AACCTGTCC CCTGAGTCTT CCCTGGCCTG TTCAGTCCCC  
 AGCAATTCCA GGGGTGCTAG AAATTTGTGTC TGTTCCTGA GAAAGCTCTT TCATGAGTTA AGCCTGAGCC CTCAAATGCC  
 ACAAGTGGCC CATGAAAAGG GAGATGGGTA GAGTCCGGCN ACCCAGTGAC AGAGTTTAGT CCTCTTTTCT CAGAATGAGC  
 40 TCACCTCAGA AGAAACCCCA AGCCATCACT GTGCGCTCTT TTCTCTCTT TCTCTCTAC AGCAGGTCTA TAACAGTCAC  
 CCTTGGAGCC CATAACATA CAGAGGAAGA AGACACATGG CAGAAGCTTG AGGTTATAAA GCAATTCCTG CATCCAAAT  
 ATAACACTTC TACTCTTAC CACGATATCA TGTACTAAA GGTGACAACA CCTCTCTCTT CCCTTTCCAC TTCCCATTTCT  
 CCTAAGCTTC TCCCTCAGGT CCTCATTGCC CTGAATTTT CTTAGACTT GGCTATAACA TGAAGCTACT CACCCTGTCC  
 CTCCCTGATC ACCTCCAAC GTCCAGAGCC CATTTCGAGG ACTGACAGTC CTTTCTTCCC TTCACAGTTG AAGGAGAAAAG  
 45 CCAGCCTGAC CCTGGCTGTG GGGACACTCC CCTTCCCTATC ACAATTCAAC TTTGTCCAC CTGGGAGAAAT GTGCCGGGTG  
 GCTGGCTGGG GAAGAACAGG TGTGTTGAAG CCGGGCTCAG ACACCTTGCA AGAGGTGAAG CTGAGACTCA TGGATCCCCA  
 GGCCTGCAGC CACTTCAGAG ACTTTGACCA CAATCTTCAG CTGTGTGTG GCAATCCAG GAAGACAAAA TCTGCTTTA  
 AGGTGATCCT CCAACTAGGT TTCCTCTCCA AAACCTCACTG TTCAGGGACC TGAATGCTCT TAGAAGGAGA TGGGGTCAGC  
 AGGTTGTGAG TCAGGTGACA GGGTGAGCAT CACAGGAATT GCTGTCTCTC CGTGGTCCAA GACAGCCTCT GACCATCCAT  
 TCCAGTCTAC TGCATTGGG GCATGGGGTG ACTGTGGA GAATGCTGTA CGGTCCCAAG AAAGGAAGAA GGGGCATCAG  
 50 AACTAGATGT ATAAGTGAGG AGCTCCACCT CCTGGGTCTG ACTTTAGGTC TCACTGTGAC TCCAAGCTGG CTGGCAGACA  
 GGAGTGGAGG ACTTCCCGGG CTCACCTTCT TCTCTCTCTC CTCCCTCTAC AGGGAGACTC TGGGGGCCCT CTTCTGTGTG  
 CTGGGGTGGC CCAAGGCATC GTATCTATG GACGGTCCGA TGCAAAGCCC CCTGCTGTCT TCAACCGAAT CTCCATTAC  
 CGGCCCTGTA TCAACAGAT CCTGCAGGCA AATTAATCCT GGATCCTGAG CCAGCCTGAA GGAAGAGCTG AACTGGACCT  
 TAGCAGCAAA GTGTGTGCAA CTCATTCTGG TTCTACCCTT GGTTCCTCA GCCACAACCC TAAGCCTCCA AGAGGTCTCC  
 55 TACAGGTAAC AGAACTTTCA ATAACTTCA GTGAAGACAC AGCTTCTAGT CGTGAGTGTG TGTCCTCTC TGCTGCTCTC  
 TTCTCTGCA CATGTGACCT GATTCCAGC CCAAGCACCA AGGA-3' (FRAG. NO:) (SEQ ID NO:11836)  
 5'-GGBGCBBCBBG-3' (FRAG. NO:1888) (SEQ ID NO:11270)  
 5'-GGBGCBBCG-3' (FRAG. NO:1889) (SEQ ID NO:11271)  
 5'-GGGGCBBCBBG CG-3' (FRAG. NO:1890) (SEQ ID NO:11272)  
 60 5'-CGTTTTTCTTCTCTC-3' (FRAG. NO:1369)(SEQ ID NO:10747)  
 5'-GCTGGTTTTCTCTTCC-3' (FRAG. NO:1370)(SEQ ID NO:10748)  
 5'-TGGCAGTGGGTGGGGGTGGGGGTGGGGTGGC-3' (FRAG. NO:1371)(SEQ ID NO:10749)  
 5'-TTCTTGTCTCTGGGGGTGTCCT-3' (FRAG. NO:1372)(SEQ ID NO:10750)  
 5'-CTTGCTCTGGGCTTTTCT-3' (FRAG. NO:1373)(SEQ ID NO:10751)  
 65 5'-CCCCTTTTCTCTCC-3' (FRAG. NO:1374)(SEQ ID NO:10752) [  
 5'-TGTCTGTTTTCTGGGG-3' (FRAG. NO:1375)(SEQ ID NO:10753)  
 5'-CTCTCTCTGCTCTGTGT-3' (FRAG. NO:1376)(SEQ ID NO:10754)  
 5'-CCTTGCCTTGGCCC-3' (FRAG. NO:1377)(SEQ ID NO:10755)  
 5'-TCTTCCCTCTCTGTCTCTGT-3' (FRAG. NO:1378)(SEQ ID NO:10756)  
 70 5'-CCCTGTGTTCGCCC-3' (FRAG. NO:1379)(SEQ ID NO:10757)  
 5'-GTCTTCCCTCTCTCTG-3' (FRAG. NO:1380)(SEQ ID NO:10758)  
 5'-ACCTCCTTTTCTCTCCG-3' (FRAG. NO:1381)(SEQ ID NO:10759)  
 5'-CTGGGTGGGGCCCTG-3' (FRAG. NO:1382)(SEQ ID NO:10760)  
 5'-CCTGTTCTCTGCTCCC-3' (FRAG. NO:1383)(SEQ ID NO:10761)  
 75 5'-TGGCTTGGGGTTTCTTCTG-3' (FRAG. NO:1384)(SEQ ID NO:10762)



5'-TGTTGCTTCTCTCTCTGTT-3' (FRAG. NO:1385)(SEQ ID NO:10763)

5'-GGCTGGCTTTCTCTCTC-3' (FRAG. NO:1386)(SEQ ID NO:10764)

5'-TTTTGTCTTCTCTGGG-3' (FRAG. NO:1387)(SEQ ID NO:10765) [1397]

5'-TGCCCCCTCTCTCTTCTTGGG-3' (FRAG. NO:1388)(SEQ ID NO:10766)

5'-TCCTTGGTGCTTGGGCTGGG-3' (FRAG. NO:1389)(SEQ ID NO:10767)

5'-GGBGCTGGBTB CTGCBGATTT CBGBGGGBBG BBCCCTGGBTB CTCBCCBGCT TCBGCTCTGG BGCBCBBGBG BBBGBGCBGC BGGGGGBGBG GBBGBBGBG CBCTTCCCB GBGBGGCTGC CTGBGCBBBT GCTGGTTTC CTTCCBGTC TTGGGTTTTB TBBCTCCCBG BBGGCBBGBG BGGGGCBBGG-3' (FRAG. NO:1891) (SEQ ID NO:11273)

# Endothelial Nitric Oxide Synthase Nucleic Acids and Antisense Oligonucleotide Fragments

- 10 5'-GCGTCTTGGG GTGCBGGGCC CBTCCTGCTG CGCCTGGGCG CTGCTGTGCG TCCGTCTGCT GGGGGGCCGG GTTGGCTGGG  
CCCTGCTTGC CGCACGACCC CGGGCCGACC CGAGGCTCGG GGGGCTGTGT TCTGGCGCTG GTGGGCTTGG GCCCTCTGG  
GGGCTGGGTT TCCTGCTGCG CCTGGGCGCT GGCCTCTTGG GGTGCGGGGC CGGGGGGCCG GGGGGCCGCT GTTCGTGGGC  
CTGGGGGTGC CTGTGGCTGC CGGTTGCCCC GGTGTGGTGC GCCGTCTGCG TGCCGGTCTG TGCTGGGTC CCCCCGCCG  
TTTCTTGGG TCCTGGCTGGG GTGCTCCGGT TCTGCTGCC GCTGCTGCC TGCTCTTCCG GCCGTGGCGC CGTGGTGGTC
- 15 CGCCCCCCTT GGCCTTCTGC TCGGGGTCTG GCTGGTGGC GGTGCCCTTG GCGGCGGTCT TCTTCTGGT GGCTCTGGGC  
CCGGCCGGTC TCGGGCGTCT CGTGTTCGCT CTGTGTCTGT TCCGGCCGCT CCTTCTCTT CCGCCGCCGC CGCTCCCGC  
CCGCTCGCTG CCTGGCCCC GCCTCTCTCT GCGCGCTGTC TCGGGCGGCG GCCTTGGCGC TCCGTTTGGG GCTGCTCTG  
GCGCTTCCGG CCTTCGGCCT GGGCGCTCTC TTCCGCTGT TCGGTGGCC CTCGTGGGCC CCTCTGGCC TCCGTTGTCC  
TGTGGTCCCC CGGCTGGTGG CCGGGCCGGT TGGGCGGGCG TGGGCGCCGG CGGTCCTCC GGGTGGCCCT TCTCCGCCG
- 20 GGTTCGCCG CTCTGCTGT TCCCTGGGCT CTCTGCTCT TCTCTGGGT GGGTGTGGG TGCCGGGGTC TCCGGGCTT  
CCCGCGCTG CTGGGCGTTC TGCGGTCTTG GGGTGTCTG TGCCCGGCT CTGTCTGCC TCCGTCTGCC TCCGTCGCC  
TCGTCCCTC CTGGGTGCGC GCGGGGCTGG TCCTGGCGTT TTGCTCTTC CTGGGCGTCT TGGGGTGCBG GCGCCBTCT  
GCTGCGCTG GCGCTGCTG TCGCTCCGTC TGCTGGGGG CCGGGGTGGC TGGGCCCTGC TTGCCGACG ACCCGGGGC  
GACCCGAGG TCGGGGGGCT GTGTTCTGGC GCTGGTGGG TGGGGCCCT CTGGGGGCTG GGTTCCTTC TGCGCTGGG
- 25 CGCTGGGCTG TTGGGTGGC GGGCCGGGG GCGCTGGGT GGGCTGGGT GGGCTGGGT GGGCTGGGT GGGCTGGGT  
CCCGGCTTGG TGGCGCCGTC CTGCTGCCG TCGTTGGCTG GGTCCCCCG CCCGTTTCTT GGGGTCCGCG TGGGTGCTC  
CGGTTCCTG TGCCGCTGCT GCCTTGTCTT TCCGGCCGTC GCGGCGTGGT GGTCCGCCCC CCTTGGCCTT CTGCTCGGG  
TCTGGCTGGT TCCGCTGCC CTGGCGGCG GTCTTCTTCC TGGTGGCTCT GGGCCCGGCC GGTCTCGGTT GTCTCGGTT
- 30 CGCTCTTGTG CTGTTCCGGC CGCTCCTTCC TCTTCCGCC CCGCCGCTCC CCGCCCGCTC GTCCGCTGG CCGGCGCTCC  
TCCTGGCCCG TGTCTCGGGC GCGCGCCTTG GCGCTCCGTT TGGGGCTGCC TCTGGCGCTT CCGGCCCTCG GCCTGGGCGC  
TCTCTTCCG CTGTGCTGGT GGCCTCTGTG GGCCTCTCT GGCCTCCGT GTCTGTGGT CCGCCGGCTG GTGGCCGGG  
CGGTGGGGC CGGTGGGGC CCGCGGGTC CTCGGGGCT CCGGGGGTCC CCGGGGGTCC CCGGGGGTCC GTGTCCCTG  
GGCTCTTCTG CCTCTCTCT GGGTGGGTGC TGGGTGCCG GGTCTCCGG CTGCCCCGC GCTGCTGGG GTTCTGCGGT  
CTTGGGGTTG TCTGTGGCCC CGCTCGTGTG GCGCTCCGTC GCGCTCGCC GGCCTCGTC CCTCTGGGT GCGCGGCGG
- 35 CTGGTCTGG CGTTTGTCT CTCTCTGG-3' (FRAG. NO:1892) (SEQ ID NO:11274)  
5'-GCGGGGCCG-3' (FRAG. NO:1893) (SEQ ID NO:11275)  
5'-CGGGGGGC-3' (FRAG. NO:1894) (SEQ ID NO:11276)  
5'-GCGCGCGGGC-3' (FRAG. NO:1895) (SEQ ID NO:11277)  
5'-CTGTGCGTCCGCTCTGCTGG (FRAG. NO:1390)(SEQ ID NO:10768)  
40 GGGGCCGGGGTGGCTGGGCCCTGCTTGCCGC (FRAG. NO:1391)(SEQ ID NO:10769)  
ACGACCCCGGCCGACCCGAG (FRAG. NO:1392)(SEQ ID NO:10770)  
GCTCGGGGGCTGTGTTCTGGCGCTGGTGGG (FRAG. NO:1393)(SEQ ID NO:10771)  
CTTGGGCCCTCTGGGGGCTGGGTT (FRAG. NO:1394)(SEQ ID NO:10772)  
TCCTGCTGCGCCTGGGCGCTG (FRAG. NO:1395)(SEQ ID NO:10773)  
45 GCGTCTTGGGGTGC (FRAG. NO:1396)(SEQ ID NO:10774)  
GGGGCCGGGGGCGCGGGG (FRAG. NO:1397)(SEQ ID NO:10775)  
GCCGCTGTCTGGGCGCTGGG (FRAG. NO:1398)(SEQ ID NO:10776)  
GGTGCCTGTGGCTGCC (FRAG. NO:1399)(SEQ ID NO:10777)  
GGTTGCCCCGGTTGGTGGC (FRAG. NO:1400)(SEQ ID NO:10778)  
50 GCCGTCTGCTGCGCGT (FRAG. NO:1401)(SEQ ID NO:10779)  
CGTTGGCTGGGTCCCCCGC (FRAG. NO:1402)(SEQ ID NO:10780)  
CCGTTCTCTGGGTGCC (FRAG. NO:1403)(SEQ ID NO:10781)  
GCGTGGGTGCTCC (FRAG. NO:1404)(SEQ ID NO:10782)  
GGTTCCTGCTGCC (FRAG. NO:1405)(SEQ ID NO:10783)  
55 CTGCTGCTTGTCTTCC (FRAG. NO:1406)(SEQ ID NO:10784)  
GGCCGTGGCGCGTGGTGGTCC (FRAG. NO:1407)(SEQ ID NO:10785)  
GCCCCCTGGCCTTCTGCTC (FRAG. NO:1408)(SEQ ID NO:10786)  
GGGGTCTGGCTGGT (FRAG. NO:1409)(SEQ ID NO:10787)  
TGCCGGTGGCCTTGGCGGC (FRAG. NO:1410)(SEQ ID NO:10788)  
60 GGTCTTCTTCTGGTG (FRAG. NO:1411)(SEQ ID NO:10789)  
GCTCTGGGCCGGCGGCTCGG (FRAG. NO:1412)(SEQ ID NO:10790)  
GCGTCTCGTGTTCG (FRAG. NO:1413)(SEQ ID NO:10791)  
CTCTGTGCTGTTCGGCCG (FRAG. NO:1414)(SEQ ID NO:10792)  
CTCTTCTCTTCCGCCGC (FRAG. NO:1415)(SEQ ID NO:10793)  
65 GCCGCTCCCCGCC (FRAG. NO:1416)(SEQ ID NO:10794)  
GCTCGTCCCTGGCCC (FRAG. NO:1417)(SEQ ID NO:10795)  
GGCCTCTCTGGCCGC (FRAG. NO:1418)(SEQ ID NO:10796)  
TGCTCGGGCGCGGCTTGGC (FRAG. NO:1419)(SEQ ID NO:10797)  
GCTCCGTTGGGGCTG (FRAG. NO:1420)(SEQ ID NO:10798)  
70 CCTTGGCGCTTCC (FRAG. NO:1421)(SEQ ID NO:10799)  
GGCCTCGGCTGGCGCTC (FRAG. NO:1422)(SEQ ID NO:10800)  
TCTCCGCTGTGC (FRAG. NO:1423)(SEQ ID NO:10801)  
TGGTGGCCCTCGTG (FRAG. NO:1424)(SEQ ID NO:10802)  
GCCCTCTGGCCTCCGGTGTCC (FRAG. NO:1425)(SEQ ID NO:10803)  
75 TGTGGTCCCCCGGCTGGT (FRAG. NO:1426)(SEQ ID NO:10804)

GGCCGGGCGGTTGGGCGGGC (FRAG. NO:1427)(SEQ ID NO:10805)  
 GTGGGCGCGGCGGCTCCTCC (FRAG. NO:1428)(SEQ ID NO:10806)  
 GGGGTGCCCTTCTCC (FRAG. NO:1429)(SEQ ID NO:10807)  
 GCCGGGGGTCCCGC (FRAG. NO:1430)(SEQ ID NO:10808)  
 5 GCTCCTGCTGTTCCCTGGGCTCTTCTGCC (FRAG. NO:1431)(SEQ ID NO:10809)  
 TCTCTCCTGGGTGGGTGCTGGGTGCCG (FRAG. NO:1432)(SEQ ID NO:10810)  
 GGGTCTCCGGGCTTG (FRAG. NO:1433)(SEQ ID NO:10811)  
 CCCCgcgctgctggcgcttctgc (FRAG. NO:1434)(SEQ ID NO:10812)  
 GGTCTTGGGGTTGTC (FRAG. NO:1435)(SEQ ID NO:10813)  
 10 TGTGGCCCCGCTCG (FRAG. NO:1436)(SEQ ID NO:10814)  
 TGTGCGCCTCCGTCGCC (FRAG. NO:1437)(SEQ ID NO:10815)  
 CGTCCGCGGCTCGTCC (FRAG. NO:1438)(SEQ ID NO:10816)  
 CCTCCTGGGTGCCG (FRAG. NO:1439)(SEQ ID NO:10817)  
 GGCGGGCTGGTCTCT (FRAG. NO:1440)(SEQ ID NO:10818)  
 15 GGCGTTTTGCTCCTTCTCTGG (FRAG. NO:1441)(SEQ ID NO:10819)  
 5'-GCGTCTTGGGGTGCBBGGGCCBCTCTGCTGCGCTGGGCGCTG-3' (FRAG. NO:1896) (SEQ ID NO:11278)

# **Inducible Nitric Synthase Nucleic Acids and Antisense Oligonucleotide Fragments**

5'-CTGCCCCBGT TTTTGBCTCT CBCBTGCCGT GGGGBGGBCB BTGGCTGCCT CCCCgggggtt TCTGCTGCTT GCTGCTTCTT  
 TCCCGTCTCC CTCTCTTCCC GTCTCCTTTT TGCTCTTTG GGTTCCTGTT GTTCTTGCC TGCTTGGTGG CGGCTTGTGC  
 20 GTTTCCTCTC TCTTCTCTTG GGTCTCCGCT TCTCGTCTG CCTTTTCTG TCTCTGTCGC GCCGTTCCTC CTCCGGCGTC  
 CTCCTGCCCT GTGCTGTTTG CCTCGGGTGG TGCGGGTGCC GGTGCTCCCG CGGCGGGCCG GCTGGTGGCC TGGGCTGTG  
 TGGTGGGGTG TGGGGCCGCT GGGTTGGGGG TGTGGTGGGC TCTTCTGTGG CCTGTGGGGC TGTGGTGTG TCTGTGGGCG  
 TGTGCTGGGT CTGGGGGCTT CCTCCCTTGT GCTGGGTGCG GCCTCCCCCG CCCCCTTCTG GGCCGGTGGC CTGGCTCCTT  
 GTGGCGCCTT CTGGCTCTTG CCCGTCTCTT CTTCGCTCG TGCTGCTGG GCTGC CATATGTATG GGAATACTGT  
 25 ATTTCAAGCA TTATAAGGAA TGAAATTATA TGCCGGTCAAT TGTGCTAAC CCTTGTAACT CTAGCACTTT GAGAGGCTGA  
 AGTGGGCAGA TCACCTGAGC TTCAGAGTTC GAGACCAGCA TGGACAACAT GGTGAAACCC AGTCTCTACC AAAACACAA  
 AAATAATTAG TGGGTGTGGT GGTGCATGCC TGTAGTCCCA GCTACTCAGG AGGCTGAGGT GGGAGGATCG CTGAGCCTG  
 GGAGGCAGAA GTTGCAATGA GCAGAGATCG TGCCACTCCG CTCCAGTCTT GGTGACAGAA TGAGACTCCA TCTCAAAAAT  
 AAATAAATAA ATAAATAAAA TAAATGAAAT GAAATTATAA GAAATTACCA CTTTTTCATG TAAGAAGTGA TCATTTCAT  
 30 TATAAGGGAA GGAATTTAAT CCTACCTGCC ATTCCACCAA AGCTTACCTA GTGCTAAAGG ATGAGGTGTT AGTAAGACCA  
 ACATCTCAGA GGCCTCTCTG TGCCAATAGC CTTCCTTCTT TTCCCTTCCA AAAACCTCAA GTGACTAGTT CAGAGGCTG  
 TCTGGAATAA TGGCATCATC TAATATCACT GGCCTTCTGG AACCTGGGCA TTTTCCAGTG TGTTCATATC TGTCAATATT  
 CCCCAGCTT CCTGGACTCC TGTACAAGC TGGAAAAGTG AGAGGATGGA CAGGGATTAA CCAGAGAGCT CCCTGCTGAG  
 GAAAAAATCT CCCAGATGCT GAAAGTGAAG CCAATGTGGT TGGCCAAATA AAACCTGGCT CCGTGGTGCC TCTGTCTTAG  
 35 CAGCCACCTT GCTGATGAAC TGCCACCTTG GACTTGGGAC CAGAAAGAGG TGGTTGGGT GAAGAGGCAC CACACAGAGT  
 GATGTAACAG CAAGATCAGG TCACCCACAG GCCCTGGCAG TCACAGTCAT AAATTAGCTA ACTGTACACA AGCTGGGGAC  
 ACTCCCTTTG GAAACCAAAA AAAAAAAGAGA CTTTATGCA AAAACAACTC TCTGGATGGC ATGGGGTGAAG  
 TATAAATACT TCTTGGCTGC CAGTGTGTTT ATAACCTTGT AGCGAGTCCA AAACCTGAGG TCCGGCCGCA GAGAACTCAG  
 CCTCATTCCT GCTTTAAAT CTCTCGGCCA CCTTTGATGA GGGGACTGGG CAGTCTTACA CAGTCCCGAA GTTCTCAAGG  
 40 CACAGGTCTC TTCTGGTTT GACTGTCTT ACCCCGGGGA GGCAGTGCAG CCAGCTGCAA GGTGAGTTGC C CATATGTATG  
 GGAATACTGT ATTTCAAGCA TTATAAGGAA TGAAATTATA GGCCGGGCAT TGTGGCTAAC CCTTGTAACT CTAGCACTTT  
 GAGAGGCTGA AGTGGGCA TCACCTGAGC TTCAGAGTTC GAGACCAGCA TGGACAACAT GGTGAAACCC AGTCTCTACC  
 AAAAAACCAA AAATATTAGC TGGGTGTGGT GGTGCTGCC TGTAGTCCCA GCTACTCAGG AGGCTGAGGT GGGAGGATCG  
 CTGAGCCTG GGAGGCAGAA GTTGCAATGA GCAGAGATCG TGCCACTCCG CTCCAGTCTT GGTGACAGAA TGAGACTCCA  
 45 TCTCAAAAAT AAATAAATAA ATAAATAAAA TAAATGAAAT GAAATTATAA GAAATTACCA CTTTTTCATG TAAGAAGTGA  
 TCATTTCAT TATAAGGAA GGAATTTAAT CCTACCTGCC ATTCCACCAA AGCTTACCTA GTGCTAAAGG ATGAGGTGTT  
 AGTAAGACCA ACATCTCAGA GGCCTCTCTG TGCCAATAGC CTTCCTTCTT TTCCCTTCCA AAAACCTCAA GTGACTAGTT  
 CAGAGGCTG TCTGGAATAA TGGCATCATC TAATATCACT GGCCTTCTGG AACCTGGGCA TTTTCCAGTG TGTTCATATC  
 TGTCAATATT CCCCAGCTT CCTGGACTCC TGTACAAGC TGGAAAAGTG AGAGGATGGA CAGGGATTAA CCAGAGAGCT  
 50 CCTGCTGAG GAAAAAATCT CCCAGATGCT GAAAGTGAAG CCAATGTGGT TGGCCAAATA AAACCTGGCT CCGTGGTGCC  
 TCTGTCTTAG CAGCCACCTT GCTGATGAAC TGCCACCTTG GACTTGGGAC CAGAAAGAGG TGGGTGGGT GAAGAGGCAC  
 CACACAGAGT GATGTAACAG CAAGATCAGG TCACCCACAG GCCCTGGCAG TCACAGTCAT AAATTAGCTA ACTGTACACA  
 AGCTGGGGAC ACTCCCTTTG GAAACCAAAA AAAAAAAGAGA CTTTATGCA AAAACAACTC TCTGGATGGC  
 ATGGGGTGAAG TATAAATACT TCTTGGCTGC CAGTGTGTTT ATAACCTTGT AGCGAGTCCA AAACCTGAGG TCCGGCCGCA  
 55 GAGAACTCAG CCTCATTCCT GCTTTAAAT CTCTCGGCCA CCTTTGATGA GGGGACTGGG CAGTCTTACA CAGTCCCGAA  
 GTTCTCAAGG CACAGGTCTC TTCTGGTTT GACTGTCTT ACCCCGGGGA GGCAGTGCAG CCAGCTGCAA GGTGAGTTGC C-3'  
 (FRAG. NO: ) (SEQ ID NO:12385)  
 5'-CTGCTTTAAA ATCTCTCGGC CACCTTTGAT GAGGGGACTG GGCAGTCTA GACAGTCCCG AAGTTCTCAA GGCACAGGTC  
 TCTTCTGGT TTGACTGTCC TTACCCCGGG GAGGCACTGC AGCCAGCTGC AAGCCCCACA GTGAAGAACA TCTGAGCTCA  
 60 AATCCAGATA AGTGACATA GTGACCTGCT TTGTAAGGCC ATAGAGATGG CCTGTCTCTG GAAATTTCTG TTCAAGACCA  
 AATTCCACCA GTATGCAATG AATGGGAAA AAGACATCAA CAACAATGTG GAGAAAGCCC CCGTGGCCAC CTCCAGTCCA  
 GTGACACAGG ATGACCTTCA GTATCAAC CTCAGCAAGC AGCAGAATGA GTCCCCGAG CCCCTCGTGG AGACGGGAAA  
 GAAGTCTCCA GAATCTCTGG TCAAGCTGGA TGAACCCCA TTGCTCTCC CACGGCATGT GAGGATCAAA AACTGGGGCA  
 GCGGGATGAC TTTCCAAGAC ACACCTTACC ATAAGGCCAA AGGATTTTAA ACTTGCAGGT CCAAACTCTG CCGTGGGTCC  
 65 ATTATGACTC CCAAAAGTTT GACCAGAGGA CCCAGGGACA AGCCTACCCC TCCAGATGAG CTTTACCTC AAGCTATCGA  
 ATTTGTCAAC CAATATTACG GCTCCTTCAA AGAGGCAAAA ATAGAGGAAC ATCTGGCCAG GGTGGAAGCG GTAACAAAGG  
 AGATAGAAAC AACAGGAACC TACCAACTGA CCGGAGATGA GCTCATCTTC GCCACCAAGC AGGCCTGGCG CAATGCCCA  
 CGCTGCATTG GAGGATCCA GTGGTCCAAC CTGACAGTCT TCGATGCCCG CAGCTGTTCC ACTGCCCGGG AAATGTTTGA  
 70 ACACATCTGC AGACACGTGC GTTACTCCAC CAACAATGGC AACATCAGGT CGGCCATCAC CGTGTTCCTC CAGCGGAGTG  
 ATGGCAAGCA CGACTTCCGG GTGTGGAATG CTGAGTCACT CCCTATGCT GGTACACAGA TGCCAGATGG CAGCATCAGA  
 GGGGACCTTG CCAACGTGGA ATTCACTCAG CTGTGATCAG ACCTGGGCTG GAAGCCCAAG TACGGCCGCT TCGATGTGGT  
 CCCCCTGGTC CTGACGGCCA ATGGCCGTGA CCCTGAGCTC TTCGAAATCC CACCTGACCT TGTGCTTGA GTGGCCATGG  
 AACATCCCAA ATACGAGTGG TTTCGGGAAC TGGAGCTAAA GTGTGACGCC CTGCCTGCAG TGGCCAAAT GCTGCTTGA  
 75 GTGGGCGGCC TGGAGTTCCC AGGGTGCCCC TTCAATGGCT GGTACATGGG CACAGAGATC GGAGTCCGGG ACTTCTGTGA  
 CGTCCAGCGC TACAACATCC TGGAGGAAGT GGGCAGGAGA ATGGCCCTG AAACCCACAA GCTGGCCTCG CTCTGGAAGG

ACCAGGCTGT CGTTGAGATC AACATTGCTG TGATCCATAG TTTTCAGAAG CAGAATGTGA CCATCATGGA CCACCACTCG  
 GCTGCAGAAT CCTTCATGAA GTACATGCCAG AATGAATACC GGTCCCCTGG GGGCTGCCCG GCAGACTGGA TTGGGCTGGT  
 CCTCCCATCT TCTGGGAGCA TCACCCCCGT GTTTCACCAAG GAGATGTCTGA ACTACGTCCT GTCCCCCTTC TACTACTATC  
 AGGTAGAGGC CTGGAAAAACC CATGTCTGGC AGGACGAGAA GCGGAGACCC AAGAGAAGAG AGATTCCATT GAAAGCTTGT  
 5 GTCAAAGCTG TGCTCTTTGC CTGTATGCTG ATGCGCAAGA CAATGGCGTC CCGAGTCAGA GTACCATCC TCTTTGCGAC  
 AGAGACAGGA AAATCAGAGG CGCTGGCCTG GGACCTGGGG GCCTTATTCA GCTGTGCCTT CAACCCCAAG GTTGTCTGCA  
 TGGATAAGTA CAGGCTGAGC TGCTGGAGG AGGAACGGCT GCTGTTGGTG GTGACCAGTA CGTTTGGCAA TGGAGACTGC  
 CCTGGCAATG GAGAGAAACT GAAGAAATCG CTCITCATGC TGAAAGAGCT CAACAACAAA TTCAGGTACG CTGTGTTTGG  
 CCTCGGCTCC AGCATGTACC CTCGGTCTG CGCCTTTGCT CATGACATTG ATCAGAAGCT GTCCCACCTG GGGGCTCTC  
 10 AGCTCACCCC GATGGGAGAA GGGGATGAGC TCAGTGGGCA GGAGGACGCC TTCCGACGCT GGGCGTGCA AACCTCAAG  
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5'-CCCCGGGG-3' (FRAG. NO:1898) (SEQ ID NO:11280)

5'-GGGGCCGCTGGG-3' (FRAG. NO:1899) (SEQ ID NO:11281)

5'-GGGGGTGTGG-3' (FRAG. NO:1900) (SEQ ID NO:11282)

5'-CTGCTCCCGGGGT-3' (FRAG. NO:1442) (SEQ ID NO:10820)

5'-TCTGTGCTGTGCTG-3' (FRAG. NO:1443) (SEQ ID NO:10821)

5'-CTTCTTTCCCGTCTCC-3' (FRAG. NO:1444) (SEQ ID NO:10822)

5'-CTTCTTTCCCGTCTCC-3' (FRAG. NO:1445) (SEQ ID NO:10823)

5'-TTTTTGCTCTTTG-3' (FRAG. NO:1446) (SEQ ID NO:10824)

5'-GGTTCCTGTGTTTCT-3' (FRAG. NO:1447) (SEQ ID NO:10825)

5'-GGCCTGCTTGGTGGC-3' (FRAG. NO:1448) (SEQ ID NO:10826)

5'-GCTTGTGCGTTTC-3' (FRAG. NO:1449) (SEQ ID NO:10827)

5'-TCTCTCTCTCTTGGGTCTCCGCTCTCTGCTGCTG-3' (FRAG. NO:1450) (SEQ ID NO:10828)

5'-TTTCTCTGCTCTGCTGCG-3' (FRAG. NO:1451) (SEQ ID NO:10829)

5'-GCCGTTCTCTCTCC-3' (FRAG. NO:1452) (SEQ ID NO:10830)

5'-GCCGCTCTCTGCCC-3' (FRAG. NO:1453) (SEQ ID NO:10831)

5'-TGTGCTGTTTGCCTCG-3' (FRAG. NO:1454) (SEQ ID NO:10832)

5'-GTGGTGGGGTCCC-3' (FRAG. NO:1455) (SEQ ID NO:10833)

5'-GGTGTCTCCCGGC-3' (FRAG. NO:1456) (SEQ ID NO:10834)

- 5'-GGGCCGGCTGGTTGCCTGGGC-3' (FRAG. NO:1457)(SEQ ID NO:10835)  
 5'-CTGTCTGGGTGGGGTGTGGGGCC-3' (FRAG. NO:1458)(SEQ ID NO:10836)  
 5'-GCTGGGTGGGGGTGTGGTG-3' (FRAG. NO:1459)(SEQ ID NO:10837)  
 5'-GGCTCTTCTGTGGCC-3' (FRAG. NO:1460)(SEQ ID NO:10838)  
 5'-TGTTGGGGCTGTGGTG-3' (FRAG. NO:1461)(SEQ ID NO:10839)  
 5'-TCTCTGTGGGCGTGTG-3' (FRAG. NO:1462)(SEQ ID NO:10840)  
 5'-CTGGGTCTTGGGGCTTC-3' (FRAG. NO:1463)(SEQ ID NO:10841)  
 5'-CTCCCTTGTGTGGG-3' (FRAG. NO:1464)(SEQ ID NO:10842)  
 5'-TGCGGCCCTCCCGC-3' (FRAG. NO:1465)(SEQ ID NO:10843)  
 5'-CCCCCTTCTGGGCC-3' (FRAG. NO:1466)(SEQ ID NO:10844)  
 5'-GGTGGCCTGGCTCCTTGTGG-3' (FRAG. NO:1467)(SEQ ID NO:10845)  
 5'-GCGCTTCTGGCTCTTG-3' (FRAG. NO:1468)(SEQ ID NO:10846)  
 5'-CCCTGTCTTCTTCGCCTCGT-3' (FRAG. NO:1469)(SEQ ID NO:10847)  
 5'-GGCTGCTGGGCTGC-3' (FRAG. NO:1470)(SEQ ID NO:10848)  
 5'-CTGCCCCBGTTTTGTCTCCTCBCBTGCCGTGGGGBGBBTTGG-3' (FRAG. NO:1901) (SEQ ID NO:11283)
- NF-κB Nucleic Acids and Antisense Oligonucleotide Fragments**  
 5'-CGGCCCTTCT CACTGGAGGC ACCGGGCAGT CCTCCATGGG AGGGTTGGGC TTGGCCGGGG CTGCCCGGTG CCTCCTTTG  
 GCTGGTCCCT CGTTGTCTT GGGCCCCG CCCCCTGCT CGGCCTCCGT GTTCTTTGGC CTCCTGCTCC GCCTGTGTG  
 TTGTCCCGTC CCCTCCTCGC TTGCGTTTC CTCTCTCTTG TCTTCCAGGC CTCTCCTCCG TCCTCGTGCT GGGGCCCGCG  
 CCGGGGGGGC GCTCGGCTCC GCGGCTTCCT CCCCCTGCTG GGGGTCCTGG TCTCCGGGGC CTGCGGCTCG CGGGCTCGGG  
 GCTGCGTGCG CCGCGCGCG CGTCCGCGGT GGGTGGCGCT GTCCCGCCGT GGTGTGTCTC CGTTCTCGTC CTGCGCGGTC  
 CTGGTCTGCC CGTGGGGTCC TGGGCGTGT GGGGGGCGTC TGGTGCCTCG TCTGCCCCGT GGGGCTTCGG GCTCGGGGCT  
 GTTCGTCGCC CCGTCCGCTC TGTGGCCTCC GGGGCTCCTC GTTTTCGCTG CTTCGGGTGT CCTTCTCGGC GTGTGGCCCC  
 GGGTCCCGC CCGTCTGGG TGGGCGGGGT CGCTGCCCTG GCGTCTGGC CCGTCTGGT GTCTGTGGT GCTTGTCTCG  
 GGTTCCTGCG CCGTGTGCT GCGGCTTCTC TGCCTCCTCG TCCGCCCTCC TGGTGGCTCG GCTGGGGGTG CCCGTGCGGG  
 GGTGGGTGTG GGGTGTTC GGGTCTCTCC CCTTCCC-3' (FRAG. NO:1902) (SEQ ID NO:11284)  
 5'-GGGCGGGGTGCG-3' (FRAG. NO:1903) (SEQ ID NO:11285)  
 5'-GCGCCGTCC-3' (FRAG. NO:1904) (SEQ ID NO:11286)  
 5'-GGGCGTGGTGG-3' (FRAG. NO:1905) (SEQ ID NO:11287)  
 5'-GTTGGGCTTGGCCGGGG-3' (FRAG. NO:1471)(SEQ ID NO:10849)  
 5'-CTGCCCGGTGCTCC-3' (FRAG. NO:1472)(SEQ ID NO:10850)  
 5'-TCTTGGCTGGTCCCTCGT-3' (FRAG. NO:1473)(SEQ ID NO:10851)  
 5'-TGCTCTGGGGCCC-3' (FRAG. NO:1474)(SEQ ID NO:10852)  
 5'-GCTCCCGCTGCTCGGCCCTCCGT-3' (FRAG. NO:1475)(SEQ ID NO:10853)  
 5'-GTTCTTTGGCCTCTTGCTCC-3' (FRAG. NO:1476)(SEQ ID NO:10854)  
 5'-GCTGTGCTCTTGCTCC-3' (FRAG. NO:1477)(SEQ ID NO:10855)  
 5'-CGTCCCTCTCGCTTGGCTTTC-3' (FRAG. NO:1478)(SEQ ID NO:10856)  
 5'-CCTCTCTCTGCTTCCA-3' (FRAG. NO:1479)(SEQ ID NO:10857)  
 5'-GGCCTTCTCTCCGCTTCCGCTGC-3' (FRAG. NO:1480)(SEQ ID NO:10858)  
 5'-TGGGGGCCCGCGCGG-3' (FRAG. NO:1481)(SEQ ID NO:10859)  
 5'-GGGGGGCGCTCGGCTCCGCGGCTTCTCCCGCG-3' (FRAG. NO:1482)(SEQ ID NO:10860)  
 5'-CTGGGGGGTCTGG-3' (FRAG. NO:1483)(SEQ ID NO:10861)  
 5'-TCTCCGGGGCCTGCGGCTCGC-3' (FRAG. NO:1484)(SEQ ID NO:10862)  
 5'-GGGCTCGGGGCTGCGTGGCC-3' (FRAG. NO:1485)(SEQ ID NO:10863)  
 5'-GCGCGCGGCGTCCGCGGTG-3' (FRAG. NO:1486)(SEQ ID NO:10864)  
 5'-GGTGGCGCTGTCCCGCC-3' (FRAG. NO:1487)(SEQ ID NO:10865)  
 5'-GTGGTGTGTCTCCGTTCTCGTCTGCGCGTC-3' (FRAG. NO:1488)(SEQ ID NO:10866)  
 5'-CTGGTCTGCCCGTGG-3' (FRAG. NO:1489)(SEQ ID NO:10867)  
 5'-GGTCTGGGCGTGGTGG-3' (FRAG. NO:1490)(SEQ ID NO:10868)  
 5'-GGGCGCTGCTGGTGC-3' (FRAG. NO:1491)(SEQ ID NO:10869)  
 5'-CTCGTCTGCCCCGTG-3' (FRAG. NO:1492)(SEQ ID NO:10870)  
 5'-GGGCTTCCGGGCTCG-3' (FRAG. NO:1493)(SEQ ID NO:10871)  
 5'-GGCTGTTCGTCCCCCTGCCGCTCTGTGGCCTCC-3' (FRAG. NO:1494)(SEQ ID NO:10872)  
 5'-GGGGCTCTCGTTTTC-3' (FRAG. NO:1495)(SEQ ID NO:10873)  
 5'-GCTGCTTCGGGTGTCTTCTC-3' (FRAG. NO:1496)(SEQ ID NO:10874)  
 5'-GGCGTGTGCCCCCGG-3' (FRAG. NO:1497)(SEQ ID NO:10875)  
 5'-GTCCCGGCCCTGTGGGCTGGGCGGGTC-3' (FRAG. NO:1498)(SEQ ID NO:10876)  
 5'-GCTGCCCTGGGCTTCTGGCCCGTCT-3' (FRAG. NO:1499)(SEQ ID NO:10877)  
 5'-GGTTGTCTGTCCGT-3' (FRAG. NO:1500)(SEQ ID NO:10878)  
 5'-GCTTGTCTCGGGTTTCTGG-3' (FRAG. NO:1501)(SEQ ID NO:10879)  
 5'-CCTCTGTGCTGGGC-3' (FRAG. NO:1502)(SEQ ID NO:10880)  
 5'-GCTTCTCTGCTCTCTGCTCC-3' (FRAG. NO:1503)(SEQ ID NO:10881)  
 5'-GCCCTCCTGGTGGCTC-3' (FRAG. NO:1504)(SEQ ID NO:10882)  
 5'-GGCTGGGGGTGCCCGTGGC-3' (FRAG. NO:1505)(SEQ ID NO:10883)  
 5'-GGGGTGGGTGTGGGTGT-3' (FRAG. NO:1506)(SEQ ID NO:10884)  
 5'-TTGGGGTCTCCCTTCCC-3' (FRAG. NO:1507)(SEQ ID NO:10885)  
 5'-CGGCCCTTCTCACTGGAGGCACCGGCAGTCTCCATGGGAGG-3' (FRAG. NO:1906)(SEQ ID NO:11288)
- Human Major Basic Protein Nucleic Acids and Antisense Oligonucleotide Fragments**  
 5'-GTT TCA TCT TGG CTT TAT CCTCT CCC CTT GTT CCT CCC CTCT CCT GCT CTG GRG TCT CCT C TTC CCT CCC TCC CCT GCC  
 GTG TTG TCT GTG GGT GTC GTT TCG CTC TTG TTG CCC TGG GCC CTT CCC TGC TGG GGG GGA GTT TCA TCT TGG GTT TCB  
 TCT TGG CTT TBT CCTCT CCC CTT GTT CCT CCC CTCT CCT GCT CTG GRG TCT CCT C TTC CCT CCC TCC CCT GCC GTG TTG  
 TCT GTG GGT GTC GTT TCG CTC TTG TTG CCC TGG GCC CTT CCC TGC TGG GGG GGB GTT TCB TCT TGG-3' (FRAG. ID:1907)  
 (SEQ ID NO:11289)  
 5'-GGG GGA GTT-3' (FRAG. ID:1908) (SEQ ID NO:11290)



- 5'-G CCC TGG GCC C-3' (FRAG. ID:1909) (SEQ ID NO:11291)  
 5'-GTT TCA TCT TGG CTT TAT CC-3' (FRAG. NO:1508) (SEQ ID NO:10886)  
 5'-TCT CCC CTT GTT CCT CCC C-3' (FRAG. NO:1509) (SEQ ID NO:10887)  
 5'-TCT CCT GCT CTG GRG TCT CCT C-3' (FRAG. NO:1510) (SEQ ID NO:10888)  
 5'-TTC CCT CCC TCC CCT GCC-3' (FRAG. NO:1511) (SEQ ID NO:10889)  
 5'-GTG TTG TCT GTG GGT GTC C-3' (FRAG. NO:1512) (SEQ ID NO:10890)  
 5'-GTT TCG CTC TTG TTG CCC-3' (FRAG. NO:1513) (SEQ ID NO:10891)  
 5'-TGG GCC CTT CCC TGC TGG-3' (FRAG. NO:1514) (SEQ ID NO:10892)  
 5'-GGG GGA GTT TCA TCT TGG-3' (FRAG. NO:1515) (SEQ ID NO:10893)  
 10 5'-GTT TCA TCT TGG CTT TAT CCTCT CCC CTT GTT CCT CCC CTCT CCT GCT CTG GRG TCT CCT C TTC CCT CCC TCC CCT GCC  
 GTG TTG TCT GTG GGT GTC GTT TCG CTC TTG TTG CCC TGG GCC CTT CCC TGC TGG GGG GGA GTT TCA TCT TGG-3' (FRAG.  
 ID:1910) (SEQ ID NO:11292)  
 5'-GTT TCB TCT TGG CTT TBT CCTCT CCC CTT GTT CCT CCC CTCT CCT GCT CTG GRG TCT CCT C TTC CCT CCC TCC CCT GCC  
 GTG TTG TCT GTG GGT GTC GTT TCG CTC TTG TTG CCC TGG GCC CTT CCC TGC TGG GGG GGB GTT TCB TCT TGG-3' (FRAG.  
 15 ID:1911) (SEQ ID NO:11293)

**Human Eosinophil Major Basic Protein Nucleic Acids and Antisense Oligonucleotide Fragments**

- 5'-GGG GGB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1516) (SEQ ID NO:10894)  
 5'-GGG GGB GTT TCB TCT TGG CTT-3' (FRAG. NO:1517) (SEQ ID NO:10895)  
 5'-GGG GGB GTT TCB TCT TGG CT-3' (FRAG. NO:1518) (SEQ ID NO:10896)  
 20 5'-GGG GGB GTT TCB TCT TGG C-3' (FRAG. NO:1519) (SEQ ID NO:10897)  
 5'-GGG GGB GTT TCB TCT TGG-3' (FRAG. NO:1520) (SEQ ID NO:10898)  
 5'-GGG GGB GTT TCB TCT TG-3' (FRAG. NO:1521) (SEQ ID NO:10899)  
 5'-GGG GGB GTT TCB TCT T-3' (FRAG. NO:1522) (SEQ ID NO:10900)  
 5'-GGG GGB GTT TCB TCT-3' (FRAG. NO:1523) (SEQ ID NO:10901)  
 25 5'-GGG GGB GTT TCB TC-3' (FRAG. NO:1524) (SEQ ID NO:10902)  
 5'-GGG GGB GTT TCB T-3' (FRAG. NO:1525) (SEQ ID NO:10903)  
 5'-GGG GGB GTT TCB-3' (FRAG. NO:1526) (SEQ ID NO:10904)  
 5'-GG GGB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1527) (SEQ ID NO:10905)  
 5'-GG GGB GTT TCB TCT TGG CTT-3' (FRAG. NO:1528) (SEQ ID NO:10906)  
 30 5'-GG GGB GTT TCB TCT TGG CT-3' (FRAG. NO:1529) (SEQ ID NO:10907)  
 5'-GG GGB GTT TCB TCT TGG C-3' (FRAG. NO:1530) (SEQ ID NO:10908)  
 5'-GG GGB GTT TCB TCT TGG-3' (FRAG. NO:1531) (SEQ ID NO:10909)  
 5'-GG GGB GTT TCB TCT TG-3' (FRAG. NO:1532) (SEQ ID NO:10910)  
 5'-GG GGB GTT TCB TCT T-3' (FRAG. NO:1533) (SEQ ID NO:10911)  
 35 5'-GG GGB GTT TCB TCT-3' (FRAG. NO:1534) (SEQ ID NO:10912)  
 5'-GG GGB GTT TCB TC-3' (FRAG. NO:1535) (SEQ ID NO:10913)  
 5'-GG GGB GTT TCB T-3' (FRAG. NO:1536) (SEQ ID NO:10914)  
 5'-G GGB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1537) (SEQ ID NO:10915)  
 5'-G GGB GTT TCB TCT TGG CTT-3' (FRAG. NO:1538) (SEQ ID NO:10916)  
 40 5'-G GGB GTT TCB TCT TGG CT-3' (FRAG. NO:1539) (SEQ ID NO:10917)  
 5'-G GGB GTT TCB TCT TGG C-3' (FRAG. NO:1540) (SEQ ID NO:10918)  
 5'-G GGB GTT TCB TCT TGG-3' (FRAG. NO:1541) (SEQ ID NO:10919)  
 5'-G GGB GTT TCB TCT TG-3' (FRAG. NO:1542) (SEQ ID NO:10920)  
 5'-G GGB GTT TCB TCT T-3' (FRAG. NO:1543) (SEQ ID NO:10921)  
 45 5'-G GGB GTT TCB TCT-3' (FRAG. NO:1544) (SEQ ID NO:10922)  
 5'-G GGB GTT TCB TC-3' (FRAG. NO:1545) (SEQ ID NO:10923)  
 5'-GGB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1546) (SEQ ID NO:10924)  
 5'-GGB GTT TCB TCT TGG CTT-3' (FRAG. NO:1547) (SEQ ID NO:10925)  
 5'-GGB GTT TCB TCT TGG CT-3' (FRAG. NO:1548) (SEQ ID NO:10926)  
 50 5'-GGB GTT TCB TCT TGG C-3' (FRAG. NO:1549) (SEQ ID NO:10927)  
 5'-GGB GTT TCB TCT TGG-3' (FRAG. NO:1550) (SEQ ID NO:10928)  
 5'-GGB GTT TCB TCT TG-3' (FRAG. NO:1551) (SEQ ID NO:10929)  
 5'-GGB GTT TCB TCT T-3' (FRAG. NO:1552) (SEQ ID NO:10930)  
 5'-GGB GTT TCB TCT-3' (FRAG. NO:1553) (SEQ ID NO:10931)  
 55 5'-GB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1554) (SEQ ID NO:10932)  
 5'-GB GTT TCB TCT TGG CTT-3' (FRAG. NO:1555) (SEQ ID NO:10933)  
 5'-GB GTT TCB TCT TGG CT-3' (FRAG. NO:1556) (SEQ ID NO:10934)  
 5'-GB GTT TCB TCT TGG C-3' (FRAG. NO:1557) (SEQ ID NO:10935)  
 5'-GB GTT TCB TCT TGG-3' (FRAG. NO:1558) (SEQ ID NO:10936)  
 60 5'-GB GTT TCB TCT TG-3' (FRAG. NO:1559) (SEQ ID NO:10937)  
 5'-GB GTT TCB TCT T-3' (FRAG. NO:1560) (SEQ ID NO:10938)  
 5'-B GTT TCB TCT TGG CTT T-3' (FRAG. NO:1561) (SEQ ID NO:10939)  
 5'-B GTT TCB TCT TGG CTT-3' (FRAG. NO:1562) (SEQ ID NO:10940)  
 5'-B GTT TCB TCT TGG CTT-3' (FRAG. NO:1563) (SEQ ID NO:10941)  
 65 5'-B GTT TCB TCT TGG CT-3' (FRAG. NO:1564) (SEQ ID NO:10942)  
 5'-B GTT TCB TCT TGG C-3' (FRAG. NO:1565) (SEQ ID NO:10943)  
 5'-B GTT TCB TCT TGG-3' (FRAG. NO:1565) (SEQ ID NO:10944)  
 5'-B GTT TCB TCT TG-3' (FRAG. NO:1567) (SEQ ID NO:10945)  
 5'-GTT TCB TCT TGG CTT T-3' (FRAG. NO:1568) (SEQ ID NO:10946)  
 70 5'-GTT TCB TCT TGG CTT-3' (FRAG. NO:1569) (SEQ ID NO:10947)  
 5'-GTT TCB TCT TGG CT-3' (FRAG. NO:1570) (SEQ ID NO:10948)  
 5'-GTT TCB TCT TGG C-3' (FRAG. NO:1571) (SEQ ID NO:10949)  
 5'-GTT TCB TCT TGG-3' (FRAG. NO:1572) (SEQ ID NO:10950)  
 5'-TT TCB TCT TGG CTT T-3' (FRAG. NO:1573) (SEQ ID NO:10951)  
 75 5'-TT TCB TCT TGG CTT-3' (FRAG. NO:1574) (SEQ ID NO:10952)

- 5'-TT TCB TCT TGG CT-3' (FRAG. NO:1575)(SEQ ID NO:10953)  
 5'-TT TCB TCT TGG C-3' (FRAG. NO:1576)(SEQ ID NO:10954)  
 5'-T TCB TCT TGG CTT T-3' (FRAG. NO:1577)(SEQ ID NO:10955)  
 5'-T TCB TCT TGG CTT-3' (FRAG. NO:1578)(SEQ ID NO:10956)  
 5 5'-T TCB TCT TGG CT-3' (FRAG. NO:1579)(SEQ ID NO:10957)  
 5'-TCB TCT TGG CTT T-3' (FRAG. NO:1580)(SEQ ID NO:10958)  
 5'-TCB TCT TGG CTT-3' (FRAG. NO:1581)(SEQ ID NO:10959)  
 5'-GGG GGB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1582)(SEQ ID NO:10960)  
 5'-GG GGB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1583)(SEQ ID NO:10961)  
 10 5'-G GGB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1584)(SEQ ID NO:10962)  
 5'-GGB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1585)(SEQ ID NO:10963)  
 5'-GB GTT TCB TCT TGG CTT T-3' (FRAG. NO:1586)(SEQ ID NO:10964)  
 5'-B GTT TCB TCT TGG CTT T-3' (FRAG. NO:1587)(SEQ ID NO:10965)  
 5'-GTT TCB TCT TGG CTT T-3' (FRAG. NO:1588)(SEQ ID NO:10966)  
 15 5'-TT TCB TCT TGG CTT T-3' (FRAG. NO:1589)(SEQ ID NO:10967)  
 5'-T TCB TCT TGG CTT T-3' (FRAG. NO:1590)(SEQ ID NO:10968)  
 5'-TCB TCT TGG CTT T-3' (FRAG. NO:1591)(SEQ ID NO:10969)  
 5'-CB TCT TGG CTT T-3' (FRAG. NO:1592)(SEQ ID NO:10970)  
 5'-GGG GGB GTT TCB TCT TGG CTT-3' (FRAG. NO:1593)(SEQ ID NO:10971)  
 20 5'-GG GGB GTT TCB TCT TGG CTT-3' (FRAG. NO:1594)(SEQ ID NO:10972)  
 5'-G GGB GTT TCB TCT TGG CTT-3' (FRAG. NO:1595)(SEQ ID NO:10973)  
 5'-GGB GTT TCB TCT TGG CTT-3' (FRAG. NO:1596)(SEQ ID NO:10974)  
 5'-GB GTT TCB TCT TGG CTT-3' (FRAG. NO:1597)(SEQ ID NO:10975)  
 5'-B GTT TCB TCT TGG CTT-3' (FRAG. NO:1598)(SEQ ID NO:10976)  
 25 5'-GTT TCB TCT TGG CTT-3' (FRAG. NO:1599)(SEQ ID NO:10977)  
 5'-TT TCB TCT TGG CTT-3' (FRAG. NO:1600)(SEQ ID NO:10978)  
 5'-T TCB TCT TGG CTT-3' (FRAG. NO:1601)(SEQ ID NO:10979)  
 5'-TCB TCT TGG CTT-3' (FRAG. NO:1602)(SEQ ID NO:10980)  
 5'-GGG GGB GTT TCB TCT TGG CT-3' (FRAG. NO:1603)(SEQ ID NO:10981)  
 30 5'-GG GGB GTT TCB TCT TGG CT-3' (FRAG. NO:1604)(SEQ ID NO:10982)  
 5'-G GGB GTT TCB TCT TGG CT-3' (FRAG. NO:1605)(SEQ ID NO:10983)  
 5'-GGB GTT TCB TCT TGG CT-3' (FRAG. NO:1606)(SEQ ID NO:10984)  
 5'-GB GTT TCB TCT TGG CT-3' (FRAG. NO:1607)(SEQ ID NO:10985)  
 5'-B GTT TCB TCT TGG CT-3' (FRAG. NO:1608)(SEQ ID NO:10986)  
 35 5'-GTT TCB TCT TGG CT-3' (FRAG. NO:1609)(SEQ ID NO:10987)  
 5'-TT TCB TCT TGG CT-3' (FRAG. NO:1610)(SEQ ID NO:10988)  
 5'-T TCB TCT TGG CT-3' (FRAG. NO:1611)(SEQ ID NO:10989)  
 5'-GGG GGB GTT TCB TCT TGG C-3' (FRAG. NO:1612)(SEQ ID NO:10990)  
 5'-GG GGB GTT TCB TCT TGG C-3' (FRAG. NO:1613)(SEQ ID NO:10991)  
 40 5'-G GGB GTT TCB TCT TGG C-3' (FRAG. NO:1614)(SEQ ID NO:10992)  
 5'-GGB GTT TCB TCT TGG C-3' (FRAG. NO:1615)(SEQ ID NO:10993)  
 5'-GB GTT TCB TCT TGG C-3' (FRAG. NO:1616)(SEQ ID NO:10994)  
 5'-B GTT TCB TCT TGG C-3' (FRAG. NO:1617)(SEQ ID NO:10995)  
 5'-GTT TCB TCT TGG C-3' (FRAG. NO:1618)(SEQ ID NO:10996)  
 45 5'-TT TCB TCT TGG C-3' (FRAG. NO:1619)(SEQ ID NO:10997)  
 5'-GGG GGB GTT TCB TCT TGG-3' (FRAG. NO:1620)(SEQ ID NO:10998)  
 5'-GG GGB GTT TCB TCT TGG-3' (FRAG. NO:1621)(SEQ ID NO:10999)  
 5'-G GGB GTT TCB TCT TGG-3' (FRAG. NO:1622)(SEQ ID NO:11000)  
 5'-GGB GTT TCB TCT TGG-3' (FRAG. NO:1623)(SEQ ID NO:11001)  
 50 5'-GB GTT TCB TCT TGG-3' (FRAG. NO:1624)(SEQ ID NO:11002)  
 5'-B GTT TCB TCT TGG-3' (FRAG. NO:1625)(SEQ ID NO:11003)  
 5'-GTT TCB TCT TGG-3' (FRAG. NO:1626)(SEQ ID NO:11004)  
 5'-GGG GGB GTT TCB TCT TG-3' (FRAG. NO:1627)(SEQ ID NO:11005)  
 5'-GG GGB GTT TCB TCT TG-3' (FRAG. NO:1628)(SEQ ID NO:11006)  
 55 5'-G GGB GTT TCB TCT TG-3' (FRAG. NO:1629)(SEQ ID NO:11007)  
 5'-GGB GTT TCB TCT TG-3' (FRAG. NO:1630)(SEQ ID NO:11008)  
 5'-GB GTT TCB TCT TG-3' (FRAG. NO:1631)(SEQ ID NO:11009)  
 5'-B GTT TCB TCT TG-3' (FRAG. NO:1632)(SEQ ID NO:11010)  
 5'-GGG GGB GTT TCB TCT T-3' (FRAG. NO:1633)(SEQ ID NO:11011)  
 60 5'-GG GGB GTT TCB TCT T-3' (FRAG. NO:1634)(SEQ ID NO:11012)  
 5'-G GGB GTT TCB TCT T-3' (FRAG. NO:1635)(SEQ ID NO:11013)  
 5'-G GGB GTT TCB TCT T-3' (FRAG. NO:1636)(SEQ ID NO:11014)  
 5'-GGB GTT TCB TCT T-3' (FRAG. NO:1637)(SEQ ID NO:11015)  
 5'-GB GTT TCB TCT T-3' (FRAG. NO:1638)(SEQ ID NO:11016)  
 65 5'-GGG GGB GTT TCB TCT-3' (FRAG. NO:1639)(SEQ ID NO:11017)  
 5'-GG GGB GTT TCB TCT-3' (FRAG. NO:1640)(SEQ ID NO:11018)  
 5'-G GGB GTT TCB TCT-3' (FRAG. NO:1641)(SEQ ID NO:11019)  
 5'-GGB GTT TCB TCT-3' (FRAG. NO:1642)(SEQ ID NO:11020)  
 5'-GGG GGB GTT TCB TC-3' (FRAG. NO:1643)(SEQ ID NO:11021)  
 70 5'-GG GGB GTT TCB TC-3' (FRAG. NO:1644)(SEQ ID NO:11022)  
 5'-G GGB GTT TCB TC-3' (FRAG. NO:1645)(SEQ ID NO:11023)  
 5'-GGG GGB GTT TCB T-3' (FRAG. NO:1646)(SEQ ID NO:11024)  
 5'-GG GGB GTT TCB T-3' (FRAG. NO:1647)(SEQ ID NO:11025)  
 5'-GGG GGB GTT TCB-3' (FRAG. NO:1648)(SEQ ID NO:11026)  
 75 5'-TCT CCC CTT GTT CCT CCC C-3' (FRAG. NO:1649)(SEQ ID NO:11027)

5'-TCT CCT GCT CTG GTG TCT CCT C-3' (FRAG. NO:1650)(SEQ ID NO:11028)

5'-TTC CCT CCC TCC CCT GCC-3' (FRAG. NO:1651)(SEQ ID NO:11029)

5'-GTG TTG TCT GTG GGT GTC C-3' (FRAG. NO:1652)(SEQ ID NO:11030)

5'-GTT TCG CTC TTG TTG CCC-3' (FRAG. NO:1653)(SEQ ID NO:10891)

5'-TGG GCC CTT CCC TGC TGG-3' (FRAG. NO:1654)(SEQ ID NO:11032)

5'-GGG GGB G-3' (FRAG. NO:1912)(SEQ ID NO:11294)

5'-GTG GGT GTC C-3' (FRAG. NO:1913) (SEQ ID NO:11295)

#### **BP-1 Nucleic Acids and Antisense Oligonucleotide Fragments**

5'-CCGTGTGTGTC BGTGGTGCTG CCCGTTTGBG GTBTGGCGCT CCBCCBBTTC CCTTTTCTCC TTGTTTCCG TTCTCTTGC

10 CGTCTGTGGT T-3' (FRAG. NO:1914) (SEQ ID NO:11296)

5'-CCCGTTTGBGGTBTGGC-3'(FRAG. NO:1915) (SEQ ID NO:11297)

5'-GCTCCBCCBBTTCCTTTTCTCC-3'(FRAG. NO:1916) (SEQ ID NO:11298)

5'-TTGTTTCCGTTTCTCTTG-3'(FRAG. NO:1917) (SEQ ID NO:11299)

5'-CCGTCTGTGGT-3'(FRAG. NO:1918) (SEQ ID NO:11300)

15 5'-CCCGTTTGAGGTATGGC-3'(FRAG. NO:1919) (SEQ ID NO:11301)

5'-GCTCCBCCAATCCCTTTTCTCC-3'(FRAG. NO:1920) (SEQ ID NO:11302)

#### **C/EBPNucleic Acids and Antisense Oligonucleotide Antisense Oligonucleotide Fragments**

5'-GGGCCCBGCCCCCGCCGCTTTTCTBGCCCC GGC-3' (FRAG. NO:1921) (SEQ ID NO:11303)

5'-GGGCCCBGCCCCCGCCGCTTTTCTBGCCCC GGC-3' (FRAG. NO:1922) (SEQ ID NO:11304)

20 5'-GGGCCCB GCCCCGCGCCTTTTCTBGCCCCG-3' (FRAG. NO:1923) (SEQ ID NO:11305)

5'-GGGCCCBGCCCCCGCCGCTTTTCTBGCCCCG-3' (FRAG. NO:1924) (SEQ ID NO:11306)

5'-GGGCCCBGCCCCCGCCGCTTTTCTBGCCCC-3' (FRAG. NO:1925) (SEQ ID NO:11307)

5'-GGGCCCBGCCCCCGCCGCTTTTCTBGCCCC-3' (FRAG. NO:1926) (SEQ ID NO:11308)

5'-GGGCCCBGCCCCCGCCGCTTTTCTBGCC-3' (FRAG. NO:1927) (SEQ ID NO:11309)

25 5'-GGGCCCBGCCCCCGCCGCTTTTCTBGCC-3' (FRAG. NO:1928) (SEQ ID NO:11310)

5'-GGGCCCBGCCCCCGCCGCTTTTCTBG-3' (FRAG. NO:1929) (SEQ ID NO:11311)

5'-GGGCCCBGCCCCCGCCGCTTTCTB-3' (FRAG. NO:1930) (SEQ ID NO:11312)

5'-GGGCCCBGCCCCCGCCGCTTTCT-3' (FRAG. NO:1931) (SEQ ID NO:11311) 1944)

5'-GGGCCCBGCCCCCGCCGCTTTTC-3' (FRAG. NO:1932) (SEQ ID NO:11314)

30 5'-GGGCCCBGCCCCCGCCGCTTTT-3' (FRAG. NO:1933) (SEQ ID NO:11315)

5'-GGGCCCBGCCCCCGCCGCTTT-3' (FRAG. NO:1934) (SEQ ID NO:11316) [1945]]

5'-GGGCCCBGCCCCCGCCGCTT-3' (FRAG. NO:1935) (SEQ ID NO:11317)

5'-GGGCCCBGCCCCCGCCGCT-3' (FRAG. NO:1936) (SEQ ID NO:11318)

5'-GGGCCCBGCCCCCGCCG-3' (FRAG. NO:1937) (SEQ ID NO:11319)

35 5'-GGGCCCBGCCCCCGCCG-3' (FRAG. NO:1938) (SEQ ID NO:11320)

5'-GGGCCCBGCCCCCGCG-3' (FRAG. NO:1939) (SEQ ID NO:11321)

5'-GGGCCCBGCCCCCGC-3' (FRAG. NO:1940) (SEQ ID NO:11322)

5'-GGGCCCBGCCCCG-3' (FRAG. NO:1941) (SEQ ID NO:11323)

5'-GGGCCCBGCCCC-3' (FRAG. NO:1942) (SEQ ID NO:11324)

40 5'-GGGCCCBGCCCC-3' (FRAG. NO:1943) (SEQ ID NO:11325)

5'-GGGCCCBGCCC-3' (FRAG. NO:1944) (SEQ ID NO:11326)

5'-GGCCCBGCCCCCGCCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1945) (SEQ ID NO:11327)

5'-GCCCBGCCCCCGCCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1946) (SEQ ID NO:11328)

5'-CCCBGCCCCCGCCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1947) (SEQ ID NO:11329)

45 5'-CCBGCCCCCGCCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1948) (SEQ ID NO:11330)

5'-CBGCCCCCGCCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1948) (SEQ ID NO:11331)

5'-BGCCCCCGCCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1950) (SEQ ID NO:11332)

5'-GCCCGCCGCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1951) (SEQ ID NO:11333)

5'-CCCCGCGCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1952) (SEQ ID NO:11334)

50 5'-CCCGCCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1953) (SEQ ID NO:11335)

5'-CCGCGCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1954) (SEQ ID NO:11336)

5'-CGCGCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1955) (SEQ ID NO:11337)

5'-GCCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1956) (SEQ ID NO:11338)

5'-CCGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1957) (SEQ ID NO:11339)

55 5'-CGCTTTTCTBGCCCCGGC-3' (FRAG. NO:1958) (SEQ ID NO:11340)

5'-GCCTTTTCTBGCCCCGGC-3' (FRAG. NO:1959) (SEQ ID NO:11341)

5'-CTTTTCTBGCCCCGGC-3' (FRAG. NO:1960) (SEQ ID NO:11342)

5'-CTTTTCTBGCCCCGGC-3' (FRAG. NO:1961) (SEQ ID NO:11343)

5'-TTTTCTBGCCCCGGC-3' (FRAG. NO:1962) (SEQ ID NO:11344)

60 5'-TTTCTBGCCCCGGC-3' (FRAG. NO:1963) (SEQ ID NO:11345)

5'-TTCTBGCCCCGGC-3' (FRAG. NO:1964) (SEQ ID NO:11346)

5'-TCTBGCCCCGGC-3' (FRAG. NO:1965) (SEQ ID NO:11347)

5'-CTBGCCCCGGC-3' (FRAG. NO:1966) (SEQ ID NO:11348)

5'-GCGBGGCTGTBCCTCGCTGGGCC-3' (FRAG. NO:1967) (SEQ ID NO:11349)

65 5'-GCGBGGCTGTBCCTCGCTGGGCC-3' (FRAG. NO:1968) (SEQ ID NO:11350)

5'-GCGBGGCTGTBCCTCGCTGGGC-3' (FRAG. NO:1969) (SEQ ID NO:11351)

5'-GCGBGGCTGTBCCTCGCTGGG-3' (FRAG. NO:1970) (SEQ ID NO:11352)

5'-GCGBGGCTGTBCCTCGCTGG-3' (FRAG. NO:1971) (SEQ ID NO:11353)

5'-GCGBGGCTGTBCCTCGTG-3' (FRAG. NO:1972) (SEQ ID NO:11354)

70 5'-GCGBGGCTGTBCCTCGT-3' (FRAG. NO:1973) (SEQ ID NO:11355)

5'-GCGBGGCTGTBCCTCGC-3' (FRAG. NO:1974) (SEQ ID NO:11356)

5'-GCGBGGCTGTBCCTCG-3' (FRAG. NO:1975) (SEQ ID NO:11357)

5'-GCGBGGCTGTBCCTC-3' (FRAG. NO:1976) (SEQ ID NO:11358)

5'-GCGBGGCTGTBCCT-3' (FRAG. NO:1977) (SEQ ID NO:11359)

5'-GCGBGGCTGTCCBC-3' (FRAG. NO:1978) (SEQ ID NO:11360)  
5'-GCGBGGCTGTCCBC-3' (FRAG. NO:1979) (SEQ ID NO:11361)  
5'-GCGBGGCTGTCCB-3' (FRAG. NO:1980) (SEQ ID NO:11362)  
5'-GCGBGGCTGTCC-3' (FRAG. NO:1981) (SEQ ID NO:11363)  
5'-GCGBGGCTGT-3' (FRAG. NO:1982) (SEQ ID NO:11364)  
5'-GCGBGGCTGTCCBCTCGCTGGGGCCC-3' (FRAG. NO:1983) (SEQ ID NO:11365)  
5'-GBGGCTGTCCBCTCGCTGGGGCCC-3' (FRAG. NO:1984) (SEQ ID NO:11366)  
5'-BGGCTGTCCBCTCGCTGGGGCCC-3' (FRAG. NO:1985) (SEQ ID NO:11367)  
5'-GGCTGTCCBCTCGCTGGGGCCC-3' (FRAG. NO:1986) (SEQ ID NO:11368)  
5'-GCTGTCCBCTCGCTGGGGCCC-3' (FRAG. NO:1987) (SEQ ID NO:11369)  
5'-CTGTCCBCTCGCTGGGGCCC-3' (FRAG. NO:1988) (SEQ ID NO:11370)  
5'-TGTCCBCTCGCTGGGGCCC-3' (FRAG. NO:1989) (SEQ ID NO:11371)  
5'-GTCBCTCGCTGGGGCCC-3' (FRAG. NO:1990) (SEQ ID NO:11372)  
5'-TCBCTCGCTGGGGCCC-3' (FRAG. NO:1991) (SEQ ID NO:11373)  
5'-CBCTCGCTGGGGCCC-3' (FRAG. NO:1992) (SEQ ID NO:11374)  
5'-BCTCGCTGGGGCCC-3' (FRAG. NO:1993) (SEQ ID NO:11375)  
5'-CCTCGCTGGGGCCC-3' (FRAG. NO:1994) (SEQ ID NO:11376)  
5'-CTCGCTGGGGCCC-3' (FRAG. NO:1995) (SEQ ID NO:11377)  
5'-TCGCTGGGGCCC-3' (FRAG. NO:1996) (SEQ ID NO:11378)  
5'-CGCTGGGGCCC-3' (FRAG. NO:1997) (SEQ ID NO:11379)  
5'-GCGCGGCGCTCBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:1998) (SEQ ID NO:11380)  
5'-GCGCGGCGCTCBTGGCGGCGCTCGGGCGGGG-3' (FRAG. NO:1999) (SEQ ID NO:11381)  
5'-GCGCGGCGCTCBTGGCGGCGCTCGGGCGGG-3' (FRAG. NO:2000) (SEQ ID NO:11382)  
5'-GCGCGGCGCTCBTGGCGGCGCTCGGGCGG-3' (FRAG. NO:2001) (SEQ ID NO:11383)  
5'-GCGCGGCGCTCBTGGCGGCGCTCGGGC-3' (FRAG. NO:2002) (SEQ ID NO:11384)  
5'-GCGCGGCGCTCBTGGCGGCGCTCGGGC-3' (FRAG. NO:2003) (SEQ ID NO:11385)  
5'-GCGCGGCGCTCBTGGCGGCGCTCGGG-3' (FRAG. NO:2004) (SEQ ID NO:11386)  
5'-GCGCGGCGCTCBTGGCGGCGCTCGG-3' (FRAG. NO:2005) (SEQ ID NO:11387)  
5'-GCGCGGCGCTCBTGGCGGCGCTCG-3' (FRAG. NO:2006) (SEQ ID NO:11388)  
5'-GCGCGGCGCTCBTGGCGGCGTC-3' (FRAG. NO:2007) (SEQ ID NO:11389)  
5'-GCGCGGCGCTCBTGGCGGCGT-3' (FRAG. NO:2008) (SEQ ID NO:11390)  
5'-GCGCGGCGCTCBTGGCGGCG-3' (FRAG. NO:2009) (SEQ ID NO:11391)  
5'-GCGCGGCGCTCBTGGCGGC-3' (FRAG. NO:2010) (SEQ ID NO:11392)  
5'-GCGCGGCGCTCBTGGCGG-3' (FRAG. NO:2011) (SEQ ID NO:11393)  
5'-GCGCGGCGCTCBTGGCG-3' (FRAG. NO:2012) (SEQ ID NO:11394)  
5'-GCGCGGCGCTCBTGGC-3' (FRAG. NO:2013) (SEQ ID NO:11395)  
5'-GCGCGGCGCTCBTG-3' (FRAG. NO:2014) (SEQ ID NO:11396)  
5'-GCGCGGCGCTCBTG-3' (FRAG. NO:2015) (SEQ ID NO:11397)  
5'-GCGCGGCGCTCBT-3' (FRAG. NO:2016) (SEQ ID NO:11398)  
5'-GCGCGGCGCTCB-3' (FRAG. NO:2017) (SEQ ID NO:11399)  
5'-GCGCGGCGCTC-3' (FRAG. NO:2018) (SEQ ID NO:11400)  
5'-GCGCGGCGCT-3' (FRAG. NO:2019) (SEQ ID NO:11401)  
5'-GCGCGGCGCTCBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2020) (SEQ ID NO:11402)  
5'-GCGGCGCTCBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2021) (SEQ ID NO:11403)  
5'-CGGCGCTCBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2022) (SEQ ID NO:11404)  
5'-GGCGCTCBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2023) (SEQ ID NO:11405)  
5'-CCGCTCBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2024) (SEQ ID NO:11406)  
5'-CCGCTCBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2025) (SEQ ID NO:11407)  
5'-CGTCTBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2026) (SEQ ID NO:11408)  
5'-GTCTBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2027) (SEQ ID NO:11409)  
5'-TCBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2028) (SEQ ID NO:11410)  
5'-CBTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2029) (SEQ ID NO:11411)  
5'-BTGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2030) (SEQ ID NO:11412)  
5'-TGGCGGCGTCGGGCGGGC-3' (FRAG. NO:2031) (SEQ ID NO:11413)  
5'-GGCGGCGTCGGGCGGGC-3' (FRAG. NO:2032) (SEQ ID NO:11414)  
5'-GCGGCGTCGGGCGGGC-3' (FRAG. NO:2033) (SEQ ID NO:11415)  
5'-CGGCGTCGGGCGGGC-3' (FRAG. NO:2034) (SEQ ID NO:11416)  
5'-GGCGTCGGGCGGGC-3' (FRAG. NO:2035) (SEQ ID NO:11417)  
5'-GCGTCGGGCGGGC-3' (FRAG. NO:2036) (SEQ ID NO:11418)  
5'-CGTCGGGCGGGC-3' (FRAG. NO:2037) (SEQ ID NO:11419)  
5'-GTCGGGCGGGC-3' (FRAG. NO:2038) (SEQ ID NO:11420)  
5'-TCGGGCGGGC-3' (FRAG. NO:2039) (SEQ ID NO:11421)  
5'-CGGCGGGC-3' (FRAG. NO:2040) (SEQ ID NO:11422)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2041) (SEQ ID NO:11423)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2042) (SEQ ID NO:11424)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2043) (SEQ ID NO:11425)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2044) (SEQ ID NO:11426)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2045) (SEQ ID NO:11427)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2046) (SEQ ID NO:11428)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2047) (SEQ ID NO:11429)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2048) (SEQ ID NO:11430)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2049) (SEQ ID NO:11431)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2050) (SEQ ID NO:11432)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2051) (SEQ ID NO:11433)  
5'-CCGCBGGCCBGGGCGCGCCGCGGGCGG-3' (FRAG. NO:2052) (SEQ ID NO:11434)

[illegible]

- 5'-CTGGCTCGGCCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2128) (SEQ ID NO:11510)  
5'-TGGCTCGGCCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2129) (SEQ ID NO:11511)  
5'-GGCTCGGCCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2130) (SEQ ID NO:11512)  
5'-GCTCGGCCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2131) (SEQ ID NO:11513)  
5'-CTCGGCCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2132) (SEQ ID NO:11514)  
5'-TCGGCCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2133) (SEQ ID NO:11515)  
5'-CGGCCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2134) (SEQ ID NO:11516)  
5'-GGCCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2135) (SEQ ID NO:11517)  
5'-GCCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2136) (SEQ ID NO:11518)  
10 5'-CCCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2137) (SEQ ID NO:11519)  
5'-CCCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2138) (SEQ ID NO:11520)  
5'-CCGGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2139) (SEQ ID NO:11521)  
5'-CGCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2140) (SEQ ID NO:11522)  
5'-GCGGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2141) (SEQ ID NO:11523)  
15 5'-CGGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2142) (SEQ ID NO:11524)  
5'-GGCCCCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2143) (SEQ ID NO:11525)  
5'-GCCCGGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2144) (SEQ ID NO:11526)  
5'-CCCGGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2145) (SEQ ID NO:11527)  
5'-CCGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2146) (SEQ ID NO:11528)  
20 5'-CGGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2147) (SEQ ID NO:11529)  
5'-GGCTTGCCCCCGGCCCGG-3' (FRAG. NO:2148) (SEQ ID NO:11530)  
5'-GCTTGCCCCCGGCCCGG-3' (FRAG. NO:2149) (SEQ ID NO:11531)  
5'-CTTGCCCCCGGCCCGG-3' (FRAG. NO:2150) (SEQ ID NO:11532)  
5'-TTGCCCCCGGCCCGG-3' (FRAG. NO:2151) (SEQ ID NO:11533)  
25 5'-TGCCCCCGGCCCGG-3' (FRAG. NO:2152) (SEQ ID NO:11534)  
5'-GCCCCCGGCCCGG-3' (FRAG. NO:2153) (SEQ ID NO:11535)  
5'-CCCGCCCGGCCCGG-3' (FRAG. NO:2154) (SEQ ID NO:11536)  
5'-CCGCCCGGCCCGG-3' (FRAG. NO:2155) (SEQ ID NO:11537)  
5'-CGCCCCCGGCCG-3' (FRAG. NO:2156) (SEQ ID NO:11538)  
30 5'-GCCCCCGGCCG-3' (FRAG. NO:2157) (SEQ ID NO:11539)  
5'-GGCGGGGGCGGCGCGCCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2158) (SEQ ID NO:11540)  
5'-GGCGGGGGCGGCGCGCCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2159) (SEQ ID NO:11541)  
5'-GGCGGGGGCGGCGCGCCTGGCTCGCCTBGGGCC-3' (FRAG. NO:2160) (SEQ ID NO:11542)  
5'-GGCGGGGGCGGCGCGCCTGGCTCGCCTBGGGC-3' (FRAG. NO:2161) (SEQ ID NO:11543)  
35 5'-GGCGGGGGCGGCGCGCCTGGCTCGCCTBGGG-3' (FRAG. NO:2162) (SEQ ID NO:11544)  
5'-GGCGGGGGCGGCGCGCCTGGCTCGCCTBGG-3' (FRAG. NO:2163) (SEQ ID NO:11545)  
5'-GGCGGGGGCGGCGCGCCTGGCTCGCCTBG-3' (FRAG. NO:2164) (SEQ ID NO:11546)  
5'-GGCGGGGGCGGCGCGCCTGGCTCGCCTB-3' (FRAG. NO:2165) (SEQ ID NO:11547)  
5'-GGCGGGGGCGGCGCGCCTGGCTCGCCT-3' (FRAG. NO:2166) (SEQ ID NO:11548)  
40 5'-GGCGGGGGCGGCGCGCCTGGCTCGCC-3' (FRAG. NO:2167) (SEQ ID NO:11549)  
5'-GGCGGGGGCGGCGCGCCTGGCTCGC-3' (FRAG. NO:2168) (SEQ ID NO:11550)  
5'-GGCGGGGGCGGCGCGCCTGGCTCG-3' (FRAG. NO:2169) (SEQ ID NO:11551)  
5'-GGCGGGGGCGGCGCGCCTGGCTC-3' (FRAG. NO:2170) (SEQ ID NO:11552)  
5'-GGCGGGGGCGGCGCGCCTGGCT-3' (FRAG. NO:2171) (SEQ ID NO:11553)  
45 5'-GGCGGGGGCGGCGCGCCTGGC-3' (FRAG. NO:2172) (SEQ ID NO:11554)  
5'-GGCGGGGGCGGCGCGCCTGG-3' (FRAG. NO:2173) (SEQ ID NO:11555)  
5'-GGCGGGGGCGGCGCGCCTG-3' (FRAG. NO:2174) (SEQ ID NO:11556)  
5'-GGCGGGGGCGGCGCGCCT-3' (FRAG. NO:2175) (SEQ ID NO:11557)  
5'-GGCGGGGGCGGCGGCGCC-3' (FRAG. NO:2176) (SEQ ID NO:11558)  
50 5'-GGCGGGGGCGGCGGCGC-3' (FRAG. NO:2177) (SEQ ID NO:11559)  
5'-GGCGGGGGCGGCGGCG-3' (FRAG. NO:2178) (SEQ ID NO:11560)  
5'-GGCGGGGGCGGCGGC-3' (FRAG. NO:2179) (SEQ ID NO:11561)  
5'-GGCGGGGGCGGCGG-3' (FRAG. NO:2180) (SEQ ID NO:11562)  
5'-GGCGGGGGCGGCG-3' (FRAG. NO:2181) (SEQ ID NO:11563)  
55 5'-GGCGGGGGCGGC-3' (FRAG. NO:2182) (SEQ ID NO:11564)  
5'-GGCGGGGGCGG-3' (FRAG. NO:2183) (SEQ ID NO:11565)  
5'-GCGGGGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2184) (SEQ ID NO:11566)  
5'-CGGGGGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2185) (SEQ ID NO:11567)  
5'-GGGGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2186) (SEQ ID NO:11568)  
60 5'-GGGGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2187) (SEQ ID NO:11569)  
5'-GGGCGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2188) (SEQ ID NO:11570)  
5'-GGGCGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2189) (SEQ ID NO:11571)  
5'-GCGGCGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2190) (SEQ ID NO:11572)  
5'-CGGCGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2191) (SEQ ID NO:11573)  
65 5'-GGCGGCGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2192) (SEQ ID NO:11574)  
5'-GCGGCGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2193) (SEQ ID NO:11575)  
5'-CGGCGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2194) (SEQ ID NO:11576)  
5'-GGCGGCGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2195) (SEQ ID NO:11577)  
5'-GCGCGGCGGCGGCGGCGGCGCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2196) (SEQ ID NO:11578)  
70 5'-CGCCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2197) (SEQ ID NO:11579)  
5'-GCCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2198) (SEQ ID NO:11580)  
5'-CCTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2199) (SEQ ID NO:11581)  
5'-CTGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2200) (SEQ ID NO:11582)  
5'-TGGCTCGCCTBGGGCCCC-3' (FRAG. NO:2201) (SEQ ID NO:11583)  
75 5'-GGCTCGCCTBGGGCCCC-3' (FRAG. NO:2202) (SEQ ID NO:11584)



- 5'-GCTCGCCTBGGGGCCCC-3' (FRAG. NO:2203) (SEQ ID NO:11585)  
 5'-CTCGCCTBGGGGCCCC-3' (FRAG. NO:2204) (SEQ ID NO:11586)  
 5'-TCGCCTBGGGGCCCC-3' (FRAG. NO:2205) (SEQ ID NO:11587)  
 5'-CGCCTBGGGGCCCC-3' (FRAG. NO:2206) (SEQ ID NO:11588)  
 5'-GCCTBGGGGCCCC-3' (FRAG. NO:2207) (SEQ ID NO:11589)  
 5'-CCTBGGGGCCCC-3' (FRAG. NO:2208) (SEQ ID NO:11590)  
 5'-CTBGGGGCCCC-3' (FRAG. NO:2209) (SEQ ID NO:11591)  
 5'-GGGTGGGCBGGCGGCC-3' (FRAG. NO:2210) (SEQ ID NO:11592)  
 5'-GGTCGGCGBBBGCTCGTCGTGGC-3' (FRAG. NO:2211) (SEQ ID NO:11593)  
 5'-GGTCGGCGBBBGCTCGTCGTGG-3' (FRAG. NO:2212) (SEQ ID NO:11594)  
 5'-GGTCGGCGBBBGCTCGTCGTG-3' (FRAG. NO:2213) (SEQ ID NO:11595)  
 5'-GGTCGGCGBBBGCTCGTCGT-3' (FRAG. NO:2214) (SEQ ID NO:11596)  
 5'-GGTCGGCGBBBGCTCGTCG-3' (FRAG. NO:2215) (SEQ ID NO:11597)  
 5'-GGTCGGCGBBBGCTCGTC-3' (FRAG. NO:2216) (SEQ ID NO:11598)  
 5'-GGTCGGCGBBBGCTCGT-3' (FRAG. NO:2217) (SEQ ID NO:11599)  
 5'-GGTCGGCGBBBGCTCG-3' (FRAG. NO:2218) (SEQ ID NO:11600)  
 5'-GGTCGGCGBBBGCTC-3' (FRAG. NO:2219) (SEQ ID NO:11601)  
 5'-GGTCGGCGBBBGCT-3' (FRAG. NO:2220) (SEQ ID NO:11602)  
 5'-GGTCGGCGBBBG-3' (FRAG. NO:2221) (SEQ ID NO:11603)  
 5'-GGTCGGCGBBBG-3' (FRAG. NO:2222) (SEQ ID NO:11604)  
 5'-GGTCGGCGBBG-3' (FRAG. NO:2223) (SEQ ID NO:11605)  
 5'-GGTCGGCGBB-3' (FRAG. NO:2224) (SEQ ID NO:11606)  
 5'-GTCGGCGBBBGCTCGTCGTGGC-3' (FRAG. NO:2225) (SEQ ID NO:11607)  
 5'-TCGGCGBBBGCTCGTCGTGGC-3' (FRAG. NO:2226) (SEQ ID NO:11608)  
 5'-CGCGBBBGCTCGTCGTGGC-3' (FRAG. NO:2227) (SEQ ID NO:11609)  
 5'-GCGBBBGCTCGTCGTGGC-3' (FRAG. NO:2228) (SEQ ID NO:11610)  
 5'-GCGBBBGCTCGTCGTGGC-3' (FRAG. NO:2229) (SEQ ID NO:11611)  
 5'-CGBBBGCTCGTCGTGGC-3' (FRAG. NO:2230) (SEQ ID NO:11612)  
 5'-GBBBGCTCGTCGTGGC-3' (FRAG. NO:2231) (SEQ ID NO:11613)  
 5'-BBBGCTCGTCGTGGC-3' (FRAG. NO:2232) (SEQ ID NO:11614)  
 5'-BGBGCTCGTCGTGGC-3' (FRAG. NO:2233) (SEQ ID NO:11615)  
 5'-GBGCTCGTCGTGGC-3' (FRAG. NO:2234) (SEQ ID NO:11616)  
 5'-BGCTCGTCGTGGC-3' (FRAG. NO:2235) (SEQ ID NO:11617)  
 5'-GCTCGTCGTGGC-3' (FRAG. NO:2236) (SEQ ID NO:11618)  
 5'-CTCGTCGTGGC-3' (FRAG. NO:2237) (SEQ ID NO:11619)  
 5'-TCGTCGTGGC-3' (FRAG. NO:2238) (SEQ ID NO:11620)  
 5'-GGGGCCCCCGCGCCGCC-3' (FRAG. NO:2239) (SEQ ID NO:11621)  
 5'-GGGGCCCCCGCGCCGCC-3' (FRAG. NO:2240) (SEQ ID NO:11622)  
 5'-GGGGCCCCCGCGCCGCC-3' (FRAG. NO:2241) (SEQ ID NO:11623)  
 5'-GGGGCCCCCGCGCCGCC-3' (FRAG. NO:2242) (SEQ ID NO:11624)  
 5'-GGGGCCCCCGCGCCGCC-3' (FRAG. NO:2243) (SEQ ID NO:11625)  
 5'-GGGGCCCCCGCGCCGCC-3' (FRAG. NO:2244) (SEQ ID NO:11626)  
 5'-GGGGCCCCCGCGCCGCC-3' (FRAG. NO:2245) (SEQ ID NO:11627)  
 5'-GGGGCCCCCGCGCCGCC-3' (FRAG. NO:2246) (SEQ ID NO:11628)  
 5'-GGGGCCCCCGCGCCGCC-3' (FRAG. NO:2247) (SEQ ID NO:11629)  
 5'-GGGGCCCCCGCGCCGCCGCC-3' (FRAG. NO:2248) (SEQ ID NO:11630)  
 5'-GGCCCCGCGCCGCCGCCGCC-3' (FRAG. NO:2249) (SEQ ID NO:11631)  
 5'-GCCCCGCGCCGCCGCCGCC-3' (FRAG. NO:2250) (SEQ ID NO:11632)  
 5'-CCCCGCGCCGCCGCCGCC-3' (FRAG. NO:2251) (SEQ ID NO:11633)  
 5'-CCCGCGCCGCCGCCGCC-3' (FRAG. NO:2252) (SEQ ID NO:11634)  
 5'-CCGCGCCGCCGCCGCC-3' (FRAG. NO:2253) (SEQ ID NO:11635)  
 5'-CGCGCCGCCGCCGCC-3' (FRAG. NO:2254) (SEQ ID NO:11636)  
 5'-GCGCGCCGCCGCCGCC-3' (FRAG. NO:2255) (SEQ ID NO:11637)  
 5'-CGCGCCGCCGCCGCC-3' (FRAG. NO:2256) (SEQ ID NO:11638)  
 5'-GCCGCCGCCGCCGCC-3' (FRAG. NO:2257) (SEQ ID NO:11639)  
 5'-GGGGCGCGCGGGCGCGCGGCC-3' (FRAG. NO:2258) (SEQ ID NO:11640)  
 5'-GGCGGGGBCGGCGCGGGCCCGGCC-3' (FRAG. NO:2259) (SEQ ID NO:11641)  
 5'-GGCGCGTCGCCGTCGCCCGCTCGGGCTCGCGC-3' (FRAG. NO:2260) (SEQ ID NO:11642)  
 5'-GCGCGGGCBBCBGCGBGCCGGCGCG-3' (FRAG. NO:2261) (SEQ ID NO:11643)  
 5'-GCGCBGCGGGCCCBCTGCGCGGGC-3' (FRAG. NO:2262) (SEQ ID NO:11644)  
 5'-GGGCGGGGTGGGCTGCCCTGCGCGGCC-3' (FRAG. NO:2263) (SEQ ID NO:11645)  
 5'-GGGCTGCTGCGCGGGGCTCCGGCGA-3' (FRAG. NO:2264) (SEQ ID NO:11646)  
 5'-CTCCGGGCGGGGCGGGCGCGGGG-3' (FRAG. NO:2265) (SEQ ID NO:11647)  
 5'-GGGCTGCCGCGGTCCGGGCCCTCTTGCCGGCG-3' (FRAG. NO:2266) (SEQ ID NO:11648)  
 5'-GCGCTCGCGCCGCTGCCGG-3' (FRAG. NO:2267) (SEQ ID NO:11649)  
 5'-GCGCCGCTTGGCCTTGTCCGCGC-3' (FRAG. NO:2268) (SEQ ID NO:11650)  
 5'-GCTGCTCCBCGCGCTGG-3' (FRAG. NO:2269) (SEQ ID NO:11651)  
 5'-GCCGGBGGCCGGCCBGGTCCCGCG-3' (FRAG. NO:2270) (SEQ ID NO:11652)  
 5'-CCCGGCGGGCGGBGGGGCGGGCTGGGC-3' (FRAG. NO:2271) (SEQ ID NO:11653)  
 5'-GTCTCTCCCGCCCGCGCGCG-3' (FRAG. NO:2272) (SEQ ID NO:11654)  
 5'-GGGCGTCCGCTCCGGGCCGTCGGG-3' (FRAG. NO:2273) (SEQ ID NO:11655)  
 5'-GCGGGCACGCGCGGCTCTGCGTCGGC-3' (FRAG. NO:2274) (SEQ ID NO:11656)
- Bradykinin Receptor Nucleic Acids and Antisense Oligonucleotide Fragments**  
 5'-GGTGBCBTG BCBTGTCCG CGCGTCCCG TTBGBGTGG GCCCGCCAGC CCAGCCACTC CACTTGGGGG CGGGTGGCCA  
 GCACGAACAG CACCCAGAGG AAGGGGGGCG GCCAGAAAGG GCAGCCGCA GGCCAGGATC AGGTCTGCTG CGGCCGAGA

TAATGGCATT CACCACGCGG CGGCCAGCG CACGCCGCGC ATCCGGCCCG GTTCTGACC TGCAGCCCC GTCTCCTTGG  
 CATTCCTGGG CCCAGTCAC TCCTCTCCCT GCCCCCTTG CTGGGCGAGG GACGGGGTG BCBTTGBGCB TGTCCGGCGG  
 GTCCCGTTBB GBGTGGGCCC GCCAGCCCAG CCACTCCACT TGGGGGCGGG TGGCCAGCAC GAACAGCACC CAGAGGAAGG  
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 5 CCAGCGCAGC CCGCGCATCC GGCCCGGGTT CTGACCTGCA GCCCCGTCT CTTGGCATT CCTGGGCCCC AGTCACTCCT  
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 GAGCAAAACGC CAGCAGGGCT GCTGTGAATT TGTGTAAGGA TTGAGGGACA GTTGTCTTC AGCATGGGCC CAGGAATGCC  
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 15 CAAGGAGGTC TGTGCCAAAG AAGAATCCAA TAAGCACATA TTGAGCACTT GCTGTATATG CAGTATTGAG CACTGTAGGC  
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 5'-GGTCCCCTTBBGBGTGGGCCC-3' (FRAG. NO:2277) (SEQ ID NO:11659)  
 5'-GCCAGCCAGCCACTCCACTTGGGGGC-3' (FRAG. NO:2278) (SEQ ID NO:11660)  
 45 5'-GGGTGGCCAGCACGAACAGCACCCAGAGGAAGGGGGGC-3' (FRAG. NO:2279) (SEQ ID NO:11661)  
 5'-GGCCCAAGAGGGCAGCCCGCAGGCCAGGATCAGGTCTGCTGCGGCC-3' (FRAG. NO:2280) (SEQ ID NO:11662)  
 5'-GGAGATAATGGCATTACACACGCGGC-3' (FRAG. NO:2281) (SEQ ID NO:11663)  
 5'-GGCCAGCGCACGCGCGCATCCGGCCC-3' (FRAG. NO:2282) (SEQ ID NO:11664)  
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 50 5'-GTCTCCTTGGCATTCTTGGGGCC-3' (FRAG. NO:2284) (SEQ ID NO:11666)  
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 5'-CTTGCTGGGGCAGGGACGG-3' (FRAG. NO:2286) (SEQ ID NO:11668)  
 5'-GGTGBCBTTTGGCBTGTGCGGCC-3' (FRAG. NO:2287) (SEQ ID NO:11669)  
 5'-GGTCCCCTTBBGBGTGGGCCC-3' (FRAG. NO:2288) (SEQ ID NO:11670)  
 55 5'-GCCAGCCAGCCACTCCACTTGGGGGC-3' (FRAG. NO:2289) (SEQ ID NO:11671)  
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 60 5'-GGGTTCTGACTTGCAGCCCCC-3' (FRAG. NO:2294) (SEQ ID NO:11676)  
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 5'-CTTGCTGGGGCAGGGACGG-3' (FRAG. NO:2297) (SEQ ID NO:11679)  
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 65 5'-CCCCTTGGGTTGTCG-3' (FRAG. NO:2299) (SEQ ID NO:11681)  
 5'-GCTCCBCCBTTTCCCTTTTCTCC-3' (FRAG. NO:2300) (SEQ ID NO:11682)  
 5'-TTGTTTCCGTTTCTCTTG-3' (FRAG. NO:2301) (SEQ ID NO:11683)  
 5'-CCGTCTGTGTTT-3' (FRAG. NO:2302) (SEQ ID NO:11684)

**B2 Adrenergic Receptor Kinase Nucleic Acids and Antisense Oligonucleotide Fragments**

70 5'-GCCCGCCCG CCAAGATGGC GGACCTGGAG GCGGTGCTGG CCGAGCTGAG CTACCTGATG GCCATGGAGA AGAGCAAGGC  
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 75 CTGAGCATGT CCAAGGCCAC TGGGGAAGA AGCAGGTGCC TCCGGATCTC TTCCAGCCAT ACATCGAAGA GATTTGTCAA



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TCTCAGAGGC TGACATGCGC TTCTATGCGG CCGAGATCAT CTTGGGCTG GAGCACATGC ACAACCGCTT CGTGGTCTAC  
COGGACCTGA AGCCAGCCAA CATCCTTCTG GACGAGCATG GCCACGTGCG GATCTCGGAC CTGGGCTG CCGTGTGACTT  
CTCCAAGAA AAGCCCCATG CCAGCGTGGG CACCCACGGG TACATGGCTC CGGAGGTCTT GCAGAAGGGC GTGGGCTACG  
10 ACAGCAGTGC CGACTGGTTC TCTCTGGGTG GCATGCTCTT CAAGTTGCTG CCGGGGACACA GCGGCTTCCG GCAGCACAAG  
ACCAAAGACA AGCATGAGAT CGACCGCATG ACGTGTGACG TGGCCGTGGA GCTGCCCGAC TCCTTCTCCC CTGAACACG  
CTCCCTGCTG GAGGGGTTGC TGCAGAGGGA TGTCAACCGG AGATTGGGCT GCCTGGGCGG AGGGGCTCAG GAGGTGAAAG  
AGAGCCCCCTT TTTCGGCTCC CTGGACTGGC AGATGGTCTT CTTCGAGAAG TACCCTCCCC CGCTGATCCC CCCACGAGGG  
GAGGTGAACG CGGCGCAGC CTTCGACATT GGCTCCTTCG ATGAGGAGGA CACAAAAGGA ATCAAGTTAC TGGACAGTGA  
15 TCAGGAGCTC TACCGCAACT TCCCCCTCAC CATCTCGAGC CGGTGGCAGC AGGAGGTGGC AGAGACTGTC TTCCGACCA  
TCAACGCTGA GACAGACCGG CTGGAGGCTC GCAAGAAAGC CAAGAAACAG CAGCTGGGCC ATGAGGAAGA CTACGCCCTG  
GGCAAGGACT GCATCATGCA TGGCTACATG TCCAAGATGG GCAACCCCTT CCTGACCCAG TGGCAGCGGC GTTACTTCTA  
CCTGTCTCCC AACCGCTCG AGTGGCGGG CGAGGCGAGA GCCTGCTGAC CATGGAGGAG ATCCAGTCCG  
TGGAGGAGAC GCAGATCAAG GAGCGCAAGT GCCTGCTCTT CAAGATCCGC GGTGGGAAAC AGTTTCAATTT GCAGTGCAT  
AGCGACCCCTG AGCTGGTGA GTGGAAGAAG GAGCTGCGCG ACGGCTACCG CGAGGCCCAG CAGCTGGTGC AGCGGGTGCC  
20 CAAGATGAAG AACAAAGCCG GCTCGCCCGT GGTGGAGCTG AGCAAGGTGC CGCTGGTCCA GCGCGGCAGT CCAACGCGCC  
TCTGACCCCT CCACCGGCT CCAGGAAGCT ACCTGGAGTA GGTGAGTCTT AGCGGATGAG TAGGAGTTGT CCACGAGGGA  
AGGTACACAG AAGGGCTTCC AGGCCAGGA AACAGCAGAG GCACAGAAGT GAGAATGGGT GGTGAGTTG GTGGGAAAC  
TCCAGGTGCA GAGGATGGTA GCGAAACAAA CTGGGACATT AAGGTCCAAG TCCTCCAAGA TCTTGACTTG CAGATTAAGG  
AGTTTGTCTA CCTAATCTGC TTTGGGAGA GTGTGGTAGC TCCTAGAGAC CCGCTAGGT CTCTCTCTC AGTAGCCCCA  
25 GAAGGCTGAG AGAGCTGCTT CTGGGTGCGA AGCAGGCACT GACTCCATCA GATCTAGATT TGGGAAAAGC ATCCCTGGTC  
AGGGCCTGCA TCAGGGCAGT GGCTGGCCAT GAGGACCCCTG AGAAGTAGAC AGATTACAGG AGATTCTCAG GAGGCCAGAC  
AGGAGACTAT GGTGACAAAT TAGATTAGAG AAGGGGAGAG AATGAAGGAG CAGTTGGGTT AAAAGAAAAC TGAGGCTGAC  
ATGGGTATAT GGTGGGAG TGACTACCA CCGACTGAGA GAGAAACCTC ACAAGCTCTG ACATGCTCTG TGTCCAGGTT  
CTGTTGGGCG TGATCCAAGA TGGTAGCCTA GAGGTGCACA GAGATGGGGG CCTTGCTTTG CAAAAGGATG CTGGCTGCTG  
30 GCCACAGACA TGGTAATGAG ATTTGAGCTT TATGTGCCA GGGCTGGGAG GAGGTTCCCTG TCACTTTGAA AGCAAAAGAG  
GGCTCTAGAG AGGGCATGTG TGAGATAGGA ATGGTCCCTT GAGACACCTG GCTTTCCCA CTCTGGGTGG CTCTCAGCAG  
GGTGGGTTTC CCTGCCCAGG CAGCACTGAA CCTCTGTGCG CTTCGGGCTG GGAGAGTTTT TACCCTAACT ACATGTGGAA  
CCATCCTGAA GGAACATCTG GATGGGATGG GGTACAGGGA AGGGAGCTGC CAAGAGTGCT GGCCAGGGAC CTGGGTCTAT  
GAGCTGGTTG GGGGGTGGG TTTGGTGCAG GGTACTTGAT CCTGAGTGGG CCTTCTGCGG CCAGGATTGG TTCTAGAGTA  
35 GGAGGGGTGG GATCGGGAT GGGGGAAGCC TGTAACCTCG GTGAGTGTG CAGGTGCCAG GTTCTGGGTG ACCTACTAAG  
GATTCTGGGT CCAGTGTGGG TCCCAGGTTA GACGTCTAG TCCTGAGTCC GTGTCCACAG TTCTGGGTGT TGAGTCTAGG  
ACAGTGATCT GGAAGTGACA GTCCAATCTA GGTCTGAGCT CTGACCCCAA GTCTAGAGTT CAGGGTCATG GTTACTAGCT  
AGGGTCAGAA TCAAGGTTGG GTTCAGTAAC CAGGATGGGA TCGAGGTCAT GGTCCAAAAT CTGGATCTGG GGACCTGTTG  
GGGGTCTGAG GTGAGTGTG CAGTCTGGGT ATGGCGTTGG AGACCCAGGG CTGTGATCTG AGGTATGGT TAGAGTCTCA  
40 GGTGGTGGGC CAAGGTTTGA GTCTGGGGTC CTGTTTGAAG TCTGGTGTCA GGTGCTGGAC TGGCTCCAAG GTCAGGGAGT  
CCGGGGTTAT AGCCAGGGTC TGAGATGAAA GTCCAGATG GTGTTTCAGAG GTCTGAATCT GTGTCTTGGT GAGCGTCCAG  
GTTCCCTGTG ATCAGCTTTG GTGTGAGGGC TGCGGCGGAG GTGGGAGGCT TGGGATCCAG AGATGTGGAC GATGTGTTGT  
GTCAGAGAAT GGGTCTCGGG TCGTCTTCGT GCGGGGTCCC TGTCGTGTTT CAGGCCCCGG TCTCCGTCCA GCATCGAGGG  
CCGAGGTCAC GGCAGGGGTC TGAGCCCGCG GTCCGAGGTC TGGTTGCGGG TCAGATTCCG CCGCGGCTCC AGGGGGCGCC  
45 GTCGCGGCC GGTCTGGCCC CTCGCGGGCT CGCTGGGCTG GTGCGGGCA GCGGGGGCCG GAGCGGGCCG CGGCTCCGGG  
GGCGCGGGCC GGGCGGCGCG GCGCGGCGCG CCGGACATGC AGTCCGCGCG GGAGCGGAGC GCGAAGCGCG GGGCGGGGCC  
CGGAGCCGCG GCCATGGGCG GCGCGCGGCT GTGAGCGGCG GCGAGCGGAG CCGCGGGCGC CAGCAGGGC CAGCGGGGAG  
CGTCCGGGCC AGAGGCCGAG CGAGCCGCGG CCGGGCGGCG CCGAGCGCGG AGCGAGCAGG AGCGGGCGCG GCGGGCGGCG  
CGCGGGGAG AGGAGCGCGC GCGGCAAGA GTGGCGGACT GGAGCGGCTG CTGGCCGACG TGAGCTACCT GAGTGGCATG  
50 GAGAAGAGCA AGGCCACGCC GCGCGCGCGC GCCAGCAAGA AGATACTGCT GCGGAGGCC AGGTGAGGAG AAGCT-3' (FRAG.  
NO: ) (SEQ ID NO: 11799)  
5'-CCAGGAAGCT ACCTGGAGGA GGTGAGTCTT AGCGGATGAG TAGGAGTTGT CCACGGAGGA AGGTACACAG AAGGGCTTCC  
AGGCCAGGA AACAGCAGAG GCACAGAAGT GAGAATGGGT GGTGAGTTG GTGGGAAAC TCAGGTGCA GAGGATGGTA  
GCGAAACAAA CTGGAGCATT AAGTCCAAG TCCTCCAAGA TCTTGACTTG CAGATTAAGG AGTTTGTCTA CCTAATCTGC  
55 TTTGGGCAGA GTGTGGTGA TCCTAGAGAC CCGTCTAGGT CTCTCTCTC AGTAGCCCA GAAGGCTGG AGAGTGCTT  
CTGGGTGCGA AGCAGGCAGT GACTCCATCA GATCTAGATT TGGGAAAAGC ATCCCTGGTC AGGGCTGCA TCAGGGCAGT  
GGCTGGCCAT GAGGACCCCTG AGAAGTAGAC AGATTACAGG AGATTCTCAG GAGGCCAGAC AGGAGACTAT GGTGACAAAT  
TAGATTAGAG AAGGGGAGAG AATGAAGGAG CAGTTGGGGT AAAAGAAAAC TGAGGCTGAC ATGGGTATAT GGGTGGCGAG  
TGACTACCA CCCACTGAGA GGAGAACCCT ACAAGCTCTG ACATGCTCTG GTTCCAGGTT CTGTTGGGGC TGATCCAAGA  
60 TGGTAGCCTA GAGGTGACCA GAGATGGGGG CCTTGCTTTG CAAAAGGATG CTGGCTGCTG GCCACAGCA TGGTAATGAG  
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TGAGATAGGA ATGCTGCTT GAGACACCTG GCTTTCCCA CTCTGGGTGG CTCTCAGCAG GGTGGGTTTC CCCTGCCAGG  
CAGCATGAA CCTCTGTGCG CTTCGGCTG GAGAGTTT TACCGTAAC ACATGTGAA CCATCTGAA GGAACATCTG  
GATGGGATGG GGTACAGGGA AGGGAGCTGC CAAGAGTGCT GGGCAGGGAC CTGGGTCTAT GAGCTGGTTG GGGGGTGGG  
65 TTTGGGTGAG GGTACTTGAT CCTGAGTGGG CCTTCTGCGG CCAGGATTGG TTCTAGAGTA GGAGGGGTGG GATCGGGAT  
GGGGGAAGCC TGTAACTCGC CTGCAGTTGT CAGGTCCAG GTTCTGGGTG ACCTACTAAG GATTCTGGT CCAGTGTGGG  
TCCCAGGTTA CCTCTGCTAG TCCTGAGTCC GTGTCCACAG TTCTGGGTGT TGAGTCTAGG ACATGATCTT GAGTGTGACA  
GTCCAATCTA GGTCTGAGTC CTGACCCAA GTCTAGAGTT CAGGGTCATG GTAGTAGCCT AGGGTCAGAA TCAAGGTTGG  
GGTCAGTAAC CAGGATGGGA TCGAGGTATC GGTGCAAAAT CTGATCTGG GAGCTGTGG TAGAGTCTCA GGTGGTGGG  
70 CAGTCTGGT AGTGTGTTGG AGACCCAGGG CTGTGATCTG AGTGTATGGT TAGAGTCTCA GGTGGTGGG CCAAGTTTGA  
GTCTGGGGTC CTGTTTGGAG TCTGGGTGCA GGTGCTGGAC TGGTCCAAG GTCAGGGAGT CCGGGGTTAT AGCCAGGGTC  
TGAGATGAAA GTCCAGATG GTGTTGAGAG GTTCTGAATCT GTGCTTGGT GAGCGTCCAG GTTCCCTGTG ATCAGGTTTG  
GTGTCAGGGC TCGGCGCCGA CTGGGAGGCC TGGGATCCAG AGATGTOACC CAGGTTGTG GTCAGAGAA GGGTCTCGGG  
TCTGCTGCT GCGGGGTCCT GTCGCTGTC CAGGCGCGG GATCGAGGG CCGAGGTGAC GCGGAGGGTC  
75 TGAGCCCGCG GTCGCGAGTC TGGTTCGGG TCAGATTCCG CCGGCGCTCC AGGGGGCGCC GTCGCGGCC GGTCTCGGCC

CTCGCGGGCT CGCTGGCGTT GTGCGCGGCA GGGCGGGCCG GAGGCGGCGG CGGCTCCGGG GCGCGGGGCC GGGCGGGCCG  
 GCGCGGGCGG CCGCGACTGC AGTCCCGGCG GGAGCGGAGC GCGAAGCGCG GGGCGGGGCC CGGAGCGGCG GCCATGGGGC  
 GCGCGCGGCT GTGAGCGGCG GCGAGCGGAG CCGCGGGCGC CGAGCAGGGC CAGGCGGGAG CGTCGGCGCC CGAGGCGGAG  
 CGAGCGCGCG CCGGGCGGGG CCGAGCGCGC AGCGAGCAGG AGCGGGCGCG GCGCGGGCGG CGGCGGGAGG AGGCGAGCGC  
 5 GCGGCCAAGA TGGCGGACCT GGAGGCGGTG CTGGCCGACG TGAGTACCT GATGGCCATG GAGAAGAGCA AGGCCACGCC  
 GCGCGCGCGC GCCAGCAAGA AGATACTGCT GCCCGAGCCC AGGTAGGAG AAGCT-3' (FRAG. NO.:) (SEQ ID NO:11798)  
 5'-GCCGCCGCG CCAAGATGGC GGACCTGGAG GCGGTGCTGG CCGACGTGAG CTACCTGATG GCCATGGAGA AGAGCAAGGC  
 CACGCGGGCC GCGCGCGCCA GCAAGAAGAT ACTGCTGCCG GAGCCCAGCA TCCGCACTGT CATGCAGAAG TACCTGGAGG  
 ACCGGGGCGA GGTGACCTTT GAGAAGATCT TTTCCAGAA GCTGGGGTAC CTGCTCTTCC GAGACTTCTG CCTGAACCAC  
 10 CTGGAGGAGG CCAGGCCCTT GGTGGAATTC TATGAGGAGA TCAAGAACTA CGAGAAGCTG GAGACGGAGG AGGAGCGTGT  
 GCGCGCGCAGC CGGGAGATCT TCGACTCATA CATCATGAAG GAGCTGCTGG CTGCTCGCA TCCCTTCTCG AAGAGTGCCA  
 CTGAGCATGT CCAAGGCCAC CTGGGGAAGA AGCAGGTGCC TCCGGATCTC TTCCAGCCAT ACATCGAAGA GATTGTGCAA  
 AACCTCCGAG GGGACGTGTT CCAGAAATTC ATTGAGGCG ATAAAGTTAC ACGGTTTTGC CAGTGGAAAG ATGTGGAGCT  
 CAACATCCAC CTGACCATGA ATGACTTCAG CGTGCATCGC ATCATTGGGC GCGGGGGCTT TGGCGAGGTC TATGGGTGCC  
 15 GGAAGGCTGA CACAGGCAAG ATGTACGCCA TGAAGTGCTT GGACAAAAG CGCATCAAGA TGAAGCAGGG GGAGACCTCG  
 GCCCTGAACG AGCGCATCAT GCTCTCGCTC GTCAGCACTG GGGACTGCC ATTCAATTGC TGCATGTCAT ACGCGTTCCA  
 CACGCGAGAC AAGCTCAGCT TCATCTGGA CCTCATCAAC GGTGGGGACC TGCATACCA CCTCTCCAG CACGGGTCT  
 TCTCAGAGGC TGACATGCGC TTCTATGCGG CCGAGATCAT CCTGGGCTCG GAGACATGC ACAACCGCTT CGTGTCTAC  
 CGGGAAGCTGA AGCCAGCCAA CATCCTTCTG GACGAGCATG GCCACGTGCG GATCTCGGAC CTGGGCGTGG CCTGTGACTT  
 20 CTCCAAGAAG AAGCCCATG CCAGCGTGGG CACCCACGGG TACATGGCTC CGGAGGTCCT CGGAGGTCCT GCAGAAGGGC GTGGCCTACG  
 ACAGCAGTGC CGACTGTTTCT TCTGTGGGT GCATGCTCTT CAAGTTGCTG CCGGGGCGCA GCCCTTCCG GCAGCACAAG  
 ACCAAAGACA AGCATGAGAT CGACCGCATG ACCTGACGTA TGGCCGTGGA GCTGCCCGAC TCCTTCTCCC CTGAACCTACG  
 CTCCTGCTG GAGGGGTTGC TGCAGAGGGA TGTCAACCGG AGATTGGGCT GCCTGGGCCG AGGGGCTCAG GAGGTGAAAG  
 AGAGCCGCTT TTTCCGCTCC CTGACTGGC AGCTGGTCTT CTGACAGAA TACCCTCCCG CGTGTACTCC CCGACGAGGG  
 25 GAGGTGAACG CCGCCGACGC CTTCGACATT GGCTCCTTCT ATGAGGAGGA CACAAAAGGA ATCAAGTTAC TGGACAGTGA  
 TCAGGAGCTC TACCGCAACT TCCCCCTCAC CATCTCGGAG CGGTGGCAGC AGGAGGTGGC AGAGACTGTC TTACGACACA  
 TCAACGCTGA GACAGACCGG CTGGAGGCTC GCAAGAAAGC CAAGAACAAG CAGCTGGGCC ATGAGGAAGC CTACGCCCTG  
 GGCAAGGACT GCATCATGCA TGGCTACATG TCCAAGATGG GCAACCCCTT CCTGACCCAG TGGCAGCGGC GGTACTTCTA  
 CCTGTTCCTC AACCGCCTCG AGTGGCGGGG CGAGGGCGAG GCCCGCAGA GCCTGCTGAC CATGGAGGAG ATCCAGTCCG  
 30 TGGAGGAGAC GCAGATCAAG GAGCGCAAGT GCTGTCTCCT CAAGATCCGC GGTGGGAAAC AGTTTCAATTT GCAGTGGCAT  
 AGCGACCTGT AGCTGGTGCA GTGGAAGAAG GAGCTGCGCG AACGCTACCG CGAGGCCCGC CAGCTGGTGC AGCGGGTGCC  
 CAAGATGAAG AACAAGCCGC GCTCGCCCGT GGTGGAGCTG AGCAAGGTGC CGTGGTCCA GCGCGGCACT GCCAACGGCC  
 TCTGACCCGC CCACCCGCT-3' (FRAG. NO.:) (SEQ ID NO:11797)

#### CCR-2 CC Chemokine Receptor Nucleic Acids and Antisense Oligonucleotide Fragments

35 5'-CTTTGTGAAG AAGGAATTGG CAACACTGAA ACCTCCAGAA CAAAGGCTGT CACTAAGGTC CCGCTGCCTT GATGGATTAT  
 ACACCTGACC TCAGTGTGAC AACAGTGACC GACTACTACT ACCCTGATAT CTCTCAAGC CCCTGTGATG CGGAACCTAT  
 TCAGACAAAT GGCAAGTTGC TCCTTGCTGT CTTTATTGTC CTCTGTTTG TATTCACTCT TCTGGGAAAC AGCCTGGTCA  
 TCCTGGTCTCT TGTGTTCTGC AAGAAGCTGA GGAGCATCAT AGATGTATAC CTCTGAACC TGGCCCTGTC TGACCTGCTT  
 TTTGCTTCT CTTTCCCTT TCGACCTAC TATCTGCTGG ACCAGTGGGT GTTGGGACT GTAATGTGCA AAGTGGTGTG  
 40 TGGCTTTTAT TACATTGGCT TCTACAGCAG CATGTTTTTC ATCACCCTCA TGAGTGTGGA CAGGTACCTG GCTGTGTGCC  
 ATGCCGTGTA TGCCCTAAAG GTGAGGACGA TCAGGATGGG CACAACGCTG TGCCCTGGCAG TATGGCTAAC GCCTATTATG  
 GCTACCATCC CATTGCTAGT GTTTTACCAA GTGGCCTCTG AAGATGGTGT TCTACAGTGT TATTCATTTT ACAATCAACA  
 GACTTTGAAG TTGAAGATCT TCACCAACTT CAAATGAAC ATTTTAGGCT TGTGTATCCC ATTACCATC TTTATGTTCT  
 GCTACATTAA AATCCTGCAC CAGCTGAAGA GGTGTCAAAA CCACAACAAG ACCAAGGCCA TCAGGTGGT GCTCATTGTG  
 45 GTCATGTGAT CTTTACTTTT CTGGGTCCCA TTCAACGTGG TTCTTTTCT CACTTCTTCT CACAGTATGC ACATCTTGA  
 TGGATGTGAG ATAAGCCAAC AGCTGACTTA TGCCACCCAT GTACAGAGAA TCATTTCCCT TACTACATGC TGTGTGAACC  
 CTGTTATCTA TGCTTTTGTG GGGGAGAAAGT TCAAGAAACA CCTCTCAGAA ATATTTCAAG AAAGTTGCAG CCAAATCTTC  
 AACTACCTAG GAAGACAAAT GCCTAGGGAG AGCTGTGAAA AGTCATCATC CTGCCAGCAG CACTCTCTCC GTTCTCCAG  
 CGTAGACTAC ATTTGTGAG GATCAATGAA GACTAAATAT AAAAAGACAT TTCTTGAATG GCATGCTAGT AGCAGTGAGC  
 50 AAAGGTGTGG GTTGTAAAGG TTTCCAAAAA AAGTATCAGCA TGAAGGATGC CGTGTGTGTT GTTGCCAAAC CTTGGAACAC  
 AATGACTGGA GACATAGTTG TGCATGCCTG GCACAACATC AAGCCTGTGA TTGTGTTTAT TGATGATGTT GAACAAGTGG  
 TGGCTTTGAG GGATCTGTA TGCCAAGTGG AAAAAAAGA TGCTCCGGA ATTCGACAGG TTATCA-3' (FRAG. NO.:) (SEQ ID  
 NO:11831)

#### CCR-4 CC Chemokine Receptor Nucleic Acids and Antisense Oligonucleotide Fragments

55 5'-TTTCATCTCT CCGGGCTTAT TTGCTGGTTT CTCCGAATGC GGGCCTTGTG TGGTTCACGC TGGATCCCCA ACGCCTAGAA  
 CAGTGCCTGG CACGCAGTTC GTCTTCTAT AAATATCGGA CTAAATGCAT CTCTGTGATG GTAATACCCA CACGGTGTG  
 TGAGAATGAA TGAGTGATTC TGTGCAAGTT CTAGTGATC TGTATCAAAA AGTACTGGTC GCTAAATTAC TCTTATAATA  
 AAGCATACTT TIAGGATAAT AAAGCACTAT TCGCGAATTG GTTACCGCTA TTATGAAATT ACTGAGCAAT ACATATCTAC  
 ATCTGATCAG TCTCCAGAAT TATGCCAAAT CCTACCTTCT TCTGAAAGTA TCTCCTAATT ATCTGCACCT GACCCATGTC  
 60 ATGCTGTGAA TGTGCAAGTA TAGCTACATC CTCCGAAGGA AGGATCTTTA CTCTTTTAC CTCTGAAAT GGTGCGTCT  
 OCTGAAAGCG GCGGGGAATG GGCGGTTGGA AGCTTGGCCC TACTTCCAGC ATTGCCGCTT ACTGGTTGGG TTACTCCAGC  
 AAGTCACTCC CTTTCCCTGG GCCTCAGTGT CTCTACTGTA GCATTCCCAG GTCTGGAATT CCATCCACTT TAGCAAGGAT  
 GGACGCGCCA CAGAGAGAGC CGTTCCTAGC CCGCGCTTCC CAGCTGTCTT CAGGCGCATC CCGCTTCCCT CAAACTTAGG  
 65 AAATGCCTCT GGGAGGTCTT GTCCGGCTCC GGACTACTA CCGACACCC GCAAAACAGCA GGTCCCCCTT GGTCTCCCA  
 GCGCGCACCC TCTCCGCCCC GCCCTGCGC CCTCTTCTCT CCGTCTGCCC CTTCTCCCCC ACCCGGCTT TCCCTCCCC  
 GCGGAGCGG CGCATGCGCC GCGCTCGGAG CGTGTGTTTA TAAAGTCCG GCGCGGCCA GAAACTTCAG TTTGTTGGCT  
 GCGGAGCAGC GTAGCAAAAGT GACGCGGAGG GCCTGAGTGC TCCAGTAGCC ACCGCATCTG GAGAACCAGG GGTACCATG  
 GAGGGGATCA GTGTAAGTCC AGTTTCAACC TGCTTTGCTA TAAATGTGTA AACGTTTGAA CTTAGAGCGC AGCCCTCTC  
 CGAGCGGCCA GAAGCGGCCA GGACATTGGA GGTACCCGTA CTCAAAAAA GGGTACCAGA AAGGAGTTT CTTGACCATG  
 70 CCTATATAGT GCGGTGTGGT GGGGGGGGAG CAGGATTGGA ATCTTTTCT CTGTGAGTGC AGGAGAAACG ACTGGAAAGA  
 GCGTTCAGT GGCTGCATGT GTCTCCCCCT TGAGTCCCGC GCGCGCGGC GGTGTGACG CTGTTTGCA ACGTAAGAAC  
 ATTCTGTGCA CAAGTGCAGA GAAGGCGTGC GCGCTGCTC GGAAGTACGA CCACCGGTCT CTTCTTGGG AGCCCGGGA  
 TGTCTGGAG CGAGTTACAT TGTCTGAATT TAGAGCGGGA GGGCGCGCTG CCTGGGCTGA CTTCCAGGA GGAGATTGCG  
 CCGCTTTAA CTTCGGGGT AAGCGCCTGG TGACTGTCT TGACACTGGG TGCGTGTTG TTAACCTCTG TGCGGCCGAC

GGAGCTGTGC CAGTCTCCCA GCACAGTAGG CAGAGGGCGG GAGAGGCGGG TGGACCCACC GCGCCGATCC TCTGAGGGGA  
 TCGAGTGGTG GCAGCAGCTA GGAGTTGATC CGCCCGCGCG CTTTGGGTTT GAGGGGGAAA CCTTCCCGCC GTCGAAGCG  
 CGCCTCTTCC CCACGGCCGC GAGTGGGTCC TGCAGTTCGA GAGTTTGGGG TCGTGCAGAG GTCAGCGGAG TGGTTTGACC  
 TCCCTTTTGA CACCGCGCAG CTGCCAGCCC TGAGATTTGC GCTCCGGGGA TAGGAGCGGG TACGGGGTGA GGGCGGGGG  
 5 CCGTTAAGAC CGCACTGGG CTGCCAGGTC GCCCGCGGA AGACTGGCAG GTGCAAGTGG GGAACCGTT TGGCTCTCTC  
 CGAGTCCAGT TGTGATGTTT AACCGTCGGT GGTTCACAGA AACCTTTTGA AACCTCTTG CTAGGGAGTT TTTGGTTTCC  
 TGCAGCGGCG CGCAATTCAA AGACGCTCGC GCGGAGCGCG CCCAGTCGCT CCCAGCACC CTGTGGGACA GAGCTGGCG  
 TGTGCCCCAG CGGAGCCCCCT GCAGCGCTGC TTGCGGGCGG TTGGCGTGGG TGTAGTGGGC AGCCGCGGCG GCCCGGGGCT  
 10 GGACGACCCG GCCCCCCGCG TGCCACCGC CTGGAGGCTT CCAGCTGCCC ACCTCCGGCC GGGTTAAGT GATCAGTGGC  
 GGGGTAATGG GAAGCCACCC GGGAGAGTGA GGAATGAAA CTTGGGGCGA GGACCACGGG TGCAGACCCC GTTACCTTCT  
 CCACCCAGGA AAATGCCCGC CTCCCTAACG TCCCAAACGC GCCAAGTGAT AAACACAGAG ATGGCAAGAG ACCCACACAC  
 CGGAGGAGCG CCCGCTTGGG GCAGGAGGTG CGGTGTGTC ATTTTCTGAC ACTCCCGCCC AATATACCCC AAGCACCAGG  
 GGGCTTCGT TTTAAGACCG CATCTCTTTT ACCCTCTTGA AGCTGCTTGA AGCCAGAAAT GGTTTGTATT TAGGCAAGCG  
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 15 CCTCTTCCCT CCCTGGGCGA AAAACTTCTT AAAAAAGTT AATCACTGCC CCTCTAGCA GCACCCACCC CACCCCCAC  
 GCCGCTGGG AGTGGCTCTT TTGTGTGTAT TTTTTTTTCT CTCTAAGGA AGGTTTTTTT TCTTCCCTCT AGTGGGCGGG  
 GCAGAGGAGT TAGCCAAGAT GTGACTTTGA AACCTCAGC GTCTCAGTGC CCTTTTGTTC TAAACAAAAG ATTITGTAAT  
 TGGTTCTACC AAAGAAGGAT ATAATGAAGT CACTATGGGA AAAGATGGGG AGGAGAGTTG TAGGATTCTA CATTAACTCT  
 CTTGTGCCCT TAGCCCACTA CTTCAGAATT TCCTGAAGAA AGCAAGCCTG AATTGGTTTT TTAATTTGCT TTAATAATTT  
 20 TTTTAACTG GGTAAATGCT TGCTGAATTG GAAGTGAATG TCCATCTCTT TGCCTCTTTT GCAGATATAC ACTTCAGATA  
 ACTACACCGA GGAATGGGCG TCAGGGGACT ATGACTCCAT GAAGGAACCC TGTTCGGTG AAGAAAATGC TAATTTCAAT  
 AAAATCTTCC TGCCACCATC CTACTCCATC ATCTTCTTAA CTGGCATTGT GGGCAATGGA TTGTCATCC TGGTCATGGG  
 TTCCCTTCTG GGCAGTTGAT GCGGTGGCAA ACTGGTACTT TGGGAACTTC CTATGCAAGG CAGTCCATCT CATCTACACA  
 25 GTCAACCTCT ACAGCAGTGT CCTCATCTG GCCTTCATCA GTCTGGACCG CTACCTGGCC ATCGTCCACG CCACCAACAG  
 TCAGAGGCCA AGGAAGCTGT TGCTGAAAAA GGTGGTCTAT GTTGGCGTCT GGATCCCTGC CCTCTGCTG ACTATTCCCG  
 ACTTCATCTT TGCCAACGTC AGTGAGGCG ATGACAGATA TATCTGTGAC CGCTTCTACC CCAATGACTT GTGGTGCTGT  
 GTGTTCCAGT TTACGCACAT CATGGTTGGC CTATCTGTC CTGTGATTGT CATCTGTCC TGTATTGCA TTTATCTCT  
 CAAGCTGTCA CACTCCAAGG GCCACCAGAA GCGCAAGGCC CTCAAGACCA CAGTCATCCT CATCTGGCT TCTTGCCT  
 30 GTTGGCTGCC TTAATCACTT GGGATCAGCA TCGACTCCIT CATCTCTCTG GAAATCATCA AGCAAGGGTG TGAGTTGAG  
 AACACTGTGC ACAAGTGGAT TTCCATCACC GAGGCCCTAG CTTTCTTCCA CTGTTGTCTG AACCCCATCC TCTATGCTTT  
 CCTGGAGCC AAATTTAAAA CCTCTGCCA GCACGCACTC ACCTCTGTGA GCAGAGGGTC CAGCCTCAAG ATCTCTCCA  
 AAGGAAAGCG AGGTGGACAT TCATCTGTTT CCATCGATC TGAGTCTTCA AGTTTCTACT CCAGCTAACA CAGATGTAAA  
 AGACTTTTTT TTAACGATA AATAACTTTT TTTAAGTTA CACATTTTTT AGATATAAAA GACTGACCAA TATTGTACAG  
 35 TTTTATGCG TGTGTGAT TTTGTCTGT GTTCTTTAG TTTTGTGAA GTTTAATGA CTTATTATA TAAATTTTTT  
 TTGTTTCATA TTGATGTGTG TCTAGGCAGG ACCTGTGGCC AAGTCTTAG TTGCTGTATG TCTCGTGTGA GGAAGTGA  
 AAAGGGAAGT GAACATTTCA GAGCGTGTAG TGAATCAGT AAAGCTAGAA ATGATCCCCA GCTGTTTATG CATAGATAAT  
 CTCTCCATTC CCGTGAACG TTTTCTCTGT TCTTAAGAGC TGATTTTGTG GTAGAAGATG GCACCTATAA CCAAGGCCA  
 AAGTGGTATA GAAATGCTGG TTTTCACTG TTCAAGAGTG GGTGTATTTC AGCACCTACA GTGTACAGTC TTGTATTAAG  
 40 TTGTTAATAA AAGTACATGT TAAACTTACT TAGTGTATG TTCTGATTTC TGTGACATT CTTTGGCTA GTAGAAGACA  
 AAAGTAATAC ATTTATGGTA TGCAAGCAC TATCTAGGT ATTTCAATTG AATATTTTAC TTAACCCCTA TCACAACTCT  
 GATAGATTCT GTTCTGTGTA CTAATTACAT TTTATAGAAG AGGAACCGGA GGCACAGAAA GCCTAAGTAA CTTGTGTAAA  
 GGCATGTAGT AAGTATCAAA TCCTGTATTT TAAACCAGGT AACATGACTT AACGAATCTG AAGCCTTCAC CACTTTAAAT  
 TCAATGGAA GTTTAGAAAT GGCCAGCCAG CACCTATTGT TATGAAAGGT CATCTTTCAG AGGATAAGCA TGTATAAAGA  
 45 AGAAAGGTA TGCAGTCGTG TTTGGATTTT ACTCCACCAT C-3' (FRAG. NO.:) (SEQ ID NO:11832)

#### CD-34 Nucleic Acids and Antisense Oligonucleotide Fragments

5'-AGGATGATGG TGATGGGGAA CTAATGGGG AAATATGGAA GTGCACAGGA AAAGTTAACA CAAGTTAGCA AAAGTTAAC  
 ATAACACAAA AAGGTCTTGC AGGAAAAAAA AAAGAAAAGA AAAGAAAGAA AAAGTCTCCA AGAATGGTTT GGACAGCCAA  
 AATGAATACT TATAGTCAGC TATACCTGCT CACTCTGAC GCTTCACTCA CACACAGCAC AGGATCTGGT GAGGCTATCA  
 50 TAAATGTGC CACATTGTGG TTAAGTTTGA CCGTATTAAC GAAATGCTCA CACTTCTAAA CTGAGGTCCT TACAGTAGAT  
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 25 GGGCGGGAAG AGCGCTCTCT GGCCAAGCCG AGTAGTGTCT TCCACTCGGT GCGTCTCTCT AGGAGCCGCG CGGGAAGGAT  
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 60 TTCTGAATAC AAAGTGATGT GTTTAAATAC TGCAATTAAT GTGATCTGA AACAC-3' (FRAG. No: ) (SEQ ID NO:11834)

#### **Eotaxin Antisense Nucleic Acids and Oligonucleotide Fragments**

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 40 GACCCCAAGA AGAAGTGGGT GCAGGATTCC ATGAAGTATC TGGACCAAAA ATCTCCAAC CCAAAGCCAT AAATAATCAC  
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 45 GGAATAC-3' (FRAG.NO.: ) (SEQ ID NO:11860)  
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# **FK-506 Binding Protein Nucleic Acids and Oligonucleotide Fragments**

10 5'-GCCAGGTCG TGTGGTCCA CGCGCCCGT CGCGCGCCC GCCGCTCAG CGTCCGCCG CGCCATGGGA GGCCGGAGCC  
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 15 CCGGTGTGTA TCCCTCCCAA TGCCACCCCT ATCTTTGACG TGGAGCTGCT CAACTTAGAG TGAAGGCAGG AAGGAACTCA  
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 AGTGTGCTAA CCTCACTGCC TCATGGCATC ATCCATTCTC TCTGCCAAG TTGCTCTGTA TGTGTCTGTC AGTGTTCATC  
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 ATGCCATAAA CCTCAAGTTA TTCA-3' (FRAG.NO.: ) (SEQ ID NO:11868)

50 5'-GCCAGGTCG TGTGGTCCA CGCGCCCGT CGCGCGCCC GCCGCTCAG CGTCCGCCG CGCCATGGGA-3' (FRAG.  
 No.: ) (SEQ ID NO:11864)

5'-GGCCGGAGCC GAGCCGGGGT CGGGCAGCAG CAGGGACCCC CCAGAGGCGG GGCTGTGGG CCGCTATGG GCGTGGAGAT  
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 55 GGTTTTGAAG AGGGTGCAGC CCAGATGAGC TTGGGGCAGA GGGCGAAGCT GACCTGCACC CCTGATGTGG CATATGGAGC  
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 GTAGTAGCCT TTCTGATGA CAGAACACAG ATCTCTTGT CGCACAATCT AACTGCCTT ACCTTCACTT AAACCACACA  
 60 CACAAGGTGC TCAGACATGA AATGTACATG CGGTACCGTA CACAGAGGGA CTGAGCCAG TTACCTTTGC TGTCACTTTC  
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 3'(FRAG. NO.: ) (SEQ ID NO:12487)

5'-GAATTCGGGC CGCCGCCAGG TCGCTGTTGG TCCACGCCGC CCGTCGCGCC GCCCGCCC GC TACGCTCCG CCGCCGCCAT  
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 65 CCGGGATGCT TGAAGATGGA AAGAAATTTG ATTCTCCCC GGACAGAAAC AAGCCCTTTA AGTTTATGCT AGGCAAGCAG  
 GAGGTGATCC GAGGTGGGA AGAAGGGGTT GCCCAGATGA GTGTGGGTCA GAGAGCCAAA CTGACTATAT CTCCAGATTA  
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 AATGACAGGA ATGGCCTCCT CCCTTAGCTC CCTGTTCTTG GATCTGCCAT GGAGGGATCT GGTGCCTCCA GACATGTGCA  
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 70 TCAGCTTTGC TTCCGACACC TCTGTTTCTT CTCTCCCTT CTCTCTGAT GTGTGTTTAC CTAAGCTATA TGCCATAAAC  
 CTCAAGTTAT TCAATTTATT TTGTTTTCAT TTTGGGGTGA AGATTCAAGT TCACTCTTTT GGATATAGGT TTCCAATTAA  
 GTACATGGTC AAGTATTAAC AGCACAAGTG GTAGGTTAAC ATTAGAATAG GAATTTGGT TGGGGGGGGG GTTTGCAAGA  
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 CAGATTTGAG GCGCTGTTGA GGAATGAACT CTCCACCAT CCCACCCACC CTCCCTTAA ACCCTCTGCC TTTGAAAGTA  
 75 AACTGAGGTG GGGATGGGGA GAGCCTTTGC TCCACCATC CCCACCCACC CTCCCTTAA ACCCTCTGCC TTTGAAAGTA



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	TTTTTTTTT	TTCATCCTGT	GGTTTTTCTA	ATGGACTTTT	AGGAATTITG	TAATCTCAT	ACITTCCAAG	CTCCACCATT
	TCCTAAATCT	TAAGAACAATT	AATTGACAGT	TTCAAATTGAA	GGTGCTGTTT	GTAGACTTAA	CACCCAGTAG	AAGCCCAGCC
	ATCATGACAA	ATCCTTGAAT	GTTCCTTAA	AAAAATGATG	CTGGTCAATG	CAGCTTCAGC	ATCTCCTGTT	TTTTGATGCT
5	TGGCTCCCTC	TGCTGATCTC	AGTTTCCTGG	CTTTTCCTCC	CTCAGCCCCT	TCTCACCCCT	TTGCTGTCCT	GTGTAGTGAT
	TGTGTGAGAA	ATCGTTGCTG	CACCCCTCCC	CCAGCACCAT	TTATGAGTCT	CAAGTTTAT	TATTGCAATA	AAAGTGCTTT
	ATGCCCGAAT TC-3' (FRAG.NO.: ) (SEQ ID NO:11866)							
	5'	GCCGCCGCCA	TGGGAGTGCA	GGTGGAAACC	ATCTCCCCAG	GAGACGGGCG	CACCTTCCCC	AAGCGCGGCC
		GGTGCACTAC	ACCGGGATGC	TTGAAGATGG	AAAGAAATTT	GATTCTCTCC	GGGACAGAAA	CAAGCCCTTT
10	TAGGCAAGCA	GGAGGTGATC	CGAGGCTGGG	AAGAAGGGGT	TGCCCGATC	AGTGTGGGTG	AGAGAGCCAA	ACTGACTATA
	TCTCCAGATT	ATGCCTATGG	TGCCACTGGG	CACCCAGGCCA	TCATCCCAAC	ACATGGCCACT	CTCGCTTTCG	ATGTGAGAGCT
	TCTAAAACTG	GAATGACAGG	AATGGCCTCC	TCCCTTAGCT	CCCTGTTCTT	GGATCTGCCR	TGGAGGGATC	TGGTGCCTCC
	AGACATGTGC	ACATGARTCC	ATATGGAGCT	TTTCTGATG	TTCCACTCCA	CTTTGTATAG	ACATCTGCCC	TGACTGAATG
	TGTTCTGTCA	CTCAGCTTTG	CTTCGGACAC	CTCTGTTTCC	TCTTCCCTTT	TCTCCTCGTA	TGTGTGTTTA	CCTAAACTAT
15	ATGCCATAAA CCTCAAGTTA TTCA-3' (FRAG.NO.: ) (SEQ ID NO:11867)							

wherein B is adenosine, or, more preferably, replaces adenosine and is an "equivalent" or a "universal" base, and adenosine A2a receptor agonist or only minimally antagonist, an adenosine A2b receptor antagonist, an adenosine A3 receptor antagonist, or an adenosine A1 receptor antagonist. Similarly, adenosine (A) may always be replaced by an "alternative", "equivalent" and/or "universal" base having a small fraction, preferably less than 0.3 of the activity of adenosine at the adenosine receptor(s), as described above.

**More sequences of examples below**

[illegible]

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gcctcgggcctccc (SEQ ID NO:11694)  
ggctggggtctgcgt (SEQ ID NO:11695)  
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gggctgggggtgctggcttgggg (SEQ ID NO:11697)  
ggggctggggcctgggccc (SEQ ID NO:11698)  
gcctgggtgggcttgggggc (SEQ ID NO:11699)  
gctgggtctctgctgttgc (SEQ ID NO:11700)  
gttgtgtggggggcc (SEQ ID NO:11701)  
10 gctgggtcggggggcctctgggtgtc (SEQ ID NO:11702)  
gccccggggccccc (SEQ ID NO:11703)  
tggtccccccctcc (SEQ ID NO:11704)  
gctccccctttcc (SEQ ID NO:11705)  
cggacgaagacagaga (SEQ ID NO:11706)  
15 ggctttgtgggtc (SEQ ID NO:11707)  
gcctgctctcccc (SEQ ID NO:11708)  
cccgccccgcchcggbbcc (SEQ ID NO:11709)  
cccgccccgcchcgg (SEQ ID NO:11710)  
cccgccccgcchcggbbcc (SEQ ID NO:11711)  
20 ccgccccgcchcgg (SEQ ID NO:11712)  
cccgccccgcctcbbg (SEQ ID NO:11713)  
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254

[illegible]

[illegible]

257





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20 **Table: Exemplary Genes and oligos**

HUMAN GENES	SEQ ID NOS. Nucleic acid (amino acid)	SEQ ID NOS. of oligos (No. of Oligonucleotide Fragments)	GENEBANK ACCESSION NOS. For the Genes
H2A histone family, member N	3285	3286-3364 (79)	AI095013
tubulin, beta polypeptide	3365	3366-3405 (40)	AI872565
ELL gene (11-19 lysine-rich leukemia gene)	3406	3407-3509 (103)	AI652901
7-dehydrocholesterol reductase	3510	3511-3592 (82)	AI652764
karyopherin alpha 2 (RAG cohort 1, importin alpha 1)	3593	3594-3680 (87)	AA489087
ADP-ribosylation factor-like 7	3681	3682-3709 (28)	AA281534
EST	3710	3711-3740 (30)	AI038433
EST	3741	3742-3808 (67)	AI122689
EST	3809	3810-3862 (53)	AI092623
ESTs	3863	3864-3936 (73)	AI095492
ESTs	3937	3938-3990 (53)	AI138216
ESTs	3991	3992-4059 (68)	AI128305
ESTs	4060	4061-4123 (63)	AI125228
ESTs	4124	4125-4181 (57)	AI041482
ESTs	4182	4183-4258 (76)	AI051839
Homo sapiens mRNA; cDNA DKFZp434A1716 (from clone DKFZp434A1716)	4259	4260-4328 (69)	AI092429
ESTs	4329	4330-4362 (33)	AI096522
ESTs	4363	4364-4421 (58)	AI122807
ESTs	4422	4423-4483 (61)	AI041212
EST	4484	4485-4544 (60)	AI125651
enolase 1, (alpha)	4545	4546-4629 (84)	AI001174
EST	4630	4631-4683 (53)	AI024215
EST	4684	4685-4729 (45)	AI034360
Homo sapiens mRNA; cDNA DKFZp564H0764 (from clone DKFZp564H0764)	4730	4731-4788 (58)	AA465687
Homo sapiens mRNA for KIAA1363 protein, partial cds	4789	4790-4853 (64)	AI085559
potassium voltage-gated channel, shaker-related subfamily, beta member 2	4854	4855-4920 (66)	AI654215
ER-associated DNAJ; ER- associated Hsp40 co- chaperone; hDj9; ERj3	4921	4922-4948 (27)	AA505075
ESTs, Weakly similar to p38 protein [H.sapiens]	4949	4950-5008 (59)	AA906703
CGI-142	5009	5010-5084 (75)	AI369870

ESTs	5085	5086-5138 (53)	AA463249
Homo sapiens clone 25058 mRNA sequence	5139	5140-5165 (26)	R38894
ESTs	5166	5167-5203 (37)	R49144
squamous cell carcinoma antigen 1	5204	5205-5290 (86)	AA398883
ESTs	5291	5292-5349 (58)	AA425700
myosin X	9 (10)	1628-2922 (1295)	NM_012334, AA187977
ESTs	5350	5351-5395 (45)	AA459692
epithelial protein lost in neoplasm beta	5396	5397-5453 (57)	AA487557
CD44 antigen (homing function and Indian blood group system)	5454	5455-5509 (55)	T69168
coagulation factor III (thromboplastin, tissue factor)	5510	5511-5588 (78)	AI313387
ESTs	5589	5590-5646 (57)	AA909635
adducin 1 (alpha)	5647	5648-5705 (58)	R00103
5' nucleotidase (CD73)	5706	5707-5767 (61)	N35316
ESTs, Moderately similar to semaphorin C [M.musculus]	5768	5769-5823 (55)	AA293300
ESTs	5824	5825-5892 (68)	AA278764
ESTs	5893	5894-5926 (33)	AA678160
calmodulin 2 (phosphorylase kinase, delta)	11 (12)	2923-3107 (185)	NM_001743, AA663941
ESTs	5927	5928-5996 (69)	R42770
high-mobility group (nonhistone chromosomal) protein 17	5997	5998-6095 (98)	H93087
chloride intracellular channel 1	6096	6097-6177 (81)	AA486518
ubiquitin carrier protein	6178	6179-6208 (30)	AA464729
transglutaminase 2 (C polypeptide, protein-glutamine- gamma-glutamyltransferase)	1 (2)	13-552 (540)	M55153, R97066
tubulin, alpha 1 (testis specific)	6209	6210-6270 (61)	AA180912
sparc/osteonectin, cwcw and kazal-like domains proteoglycan (testican)	6271	6272-6343 (72)	AA436142
proteasome (prosome, macropain) 26S subunit, non- ATPase, 2	6344	6345-6413 (69)	H05893
tubulin, beta polypeptide	6414	6415-6485 (71)	H37989
filamin B, beta (actin-binding protein-278)	6486	6487-6551 (65)	AA486238
stanniocalcin	5 (6)	677-1323 (647)	NM_003155, AA085318
low density lipoprotein receptor (familial hypercholesterolemia)	6552	6553-6609 (57)	AA504461
plectin 1, intermediate filament binding protein, 500kD	6610	6611-6683 (73)	AA448400
S100 calcium-binding protein A2	3 (4)	553-676 (124)	BC002829, AA458884
Immediate early response 3	6684	6685-6735 (51)	AA480815
calpain, large polypeptide L2	6736	6737-6831 (95)	AA102454
pleckstrin homology-like domain, family A, member 1	6832	6833-6900 (68)	AA258396
melanoma adhesion molecule	6901	6902-6979 (78)	AA497002
CD44 antigen (homing function and Indian blood group system)	6980	6981-7069 (89)	AA282906
programmed cell death 5	7070	7071-7159 (89)	AA156940
hexokinase 1	7160	7161-7209 (49)	AA485272
vascular endothelial growth factor	7210	7211-7290 (80)	R19956
integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	7291	7292-7396 (105)	AA463610
calumenin	7397	7398-7471 (74)	R78585
syntaxin 11	7472	7473-7526 (54)	R33851
diphtheria toxin receptor	7527	7528-7578 (51)	R14663

(heparin-binding epidermal growth factor-like growth factor) Fn14 for type I transmembrane protein	7579	7580-7632 (53)	R33355
Nef-associated factor 1	7633	7634-7694 (61)	T64626
high-mobility group (nonhistone chromosomal) protein isoforms I and Y	7695	7696-7753 (58)	AA448261
catechol-O-methyltransferase	7754	7755-7796 (42)	R44202
C-terminal binding protein 1	7797	7798-7864 (67)	W81570
collagen, type XVII, alpha 1	7865	7866-7932 (67)	AA128561
ESTs	7933	7934-8029 (96)	N58473
farnesyl-diphosphate farnesyltransferase 1	8030	8031-8107 (77)	AA679352
RNA helicase-related protein	8108	8109-8147 (39)	N55459
interferon stimulated gene (20kD)	8148	8149-8230 (82)	AA150500
steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)	8231	8232-8283 (52)	H16833
prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	8284	8285-8345 (61)	AA644211
laminin, alpha 3 (nicein (150kD), kalinin (165kD), BM600 (150kD), epilegrin)	8346	8347-8440 (94)	AA001432
collagen, type XVII, alpha 1	8441	8442-8494 (53)	H87536
keratin 18	8495	8496-8601 (106)	AA664179
heparan sulfate (glucosamine) 3-O-sulfotransferase 1	8602	8603-8652 (50)	H86812
tubulin, alpha 2	8653	8654-8765 (112)	AA626698
adenylyl cyclase-associated protein	8766	8767-8833 (67)	R37953
forkhead box D1	8834	8835-8897 (63)	AA069372
cathepsin C	7 (8)	1324-1627 (304)	NM_001814, AA644088
ESTs, Highly similar to AF151802_1 CGI-44 protein [H.sapiens]	8898	8899-8985 (87)	T74688
ribonucleotide reductase M2 polypeptide	8986	8987-9056 (70)	AA187351
laminin, gamma 2 (nicein (100kD), kalinin (105kD), BM600 (100kD), Herlitz junctional epidermolysis bullosa))	9057	9058-9133 (76)	AA677534
Homo sapiens mRNA; cDNA DKFZp586P1622 (from clone DKFZp586P1622)	9134	9135-9221 (87)	T59658
ESTs, Weakly similar to /prediction	9222	9223-9289 (67)	AA284245
lactate dehydrogenase A	9290	9291-9369 (79)	H05914
Total	98 genes	9369 (9277)	

(GENBANK ACCESSION NO. M55153)

5 AACAGGCGTGACGCCAGTTCTAAACTTGAAACAAAAACAACTTCAAAGTACACCAAAATAGAACCTCCTTAAAGCATAAATCTCA  
CGGAGGGTCTCGGCCGCCAGTGGAAGGAGCCACCGCCCCCGCCCGACCATGGCCGAGGAGCTGGTCTTAGAGAGGTGTGATCTGG  
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GACCTTGCACTTTGAGGGCCGCAACTACCAGGCCAGTGTAGACAGTCTCACCTTCAGTGTCTGTGACCGGCCAGCCCTAGGCCAGG  
AGGCCGGGACCAAGGCCCGTTTCCACTAAGAGATGCTGTGGAGGAGGGTGACTGGACAGCCACCGTGGTGGACAGCAAGACTG  
10 CACCTCTCGCTGCAGCTCACACCCCGGCCAACGCCCCCATCGGCCTGTATCGCCTCAGCCTGGAGGCCTCCACTGGCTACCAGGG  
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CAGCAGCCCGCTACGTGGGCCGGGTGGGTAGTGGCATGGTCAACTGCAACGATGACCAGGGTGTGCTGCTGGGACGCTGGGACA  
15 ACAACTACGGGACGGCGTCAGCCCCATGTCCTGGATCGGCAGCGTGACATCCTGCGGCGCTGGAAGAACCACGGCTGCCAGCGC  
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 5 AAATACCCAGAGGGTCTCAGAGGAGAGGGGCTTCAAGGGCGAACCACCTGAACAACTGGCCGAGAAAGGAGAGACA  
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 20 ACCATTGTGAAGCACTACTATGTGCTGGGTGCCTCCACACTTGTCTGGGGCTCAGCGGGCCTCAACCCATTATTAACCATGGGA  
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 25 TCAGAGGAGTGATTGAACCTGCTCATCTCCAAGGATCCTCTCCACTCCATGTTTGAATACACAATTCC  
 (SEQ ID NO: 1)

Amino acid sequence for G-protein G-alpha H (GENBANK ACCESSION No. M55153)

MetAlaGluGluValLeuGluArgCysAspLeuGluGluThrAsnGlyArgAspHisHisThrAlaAspLeuCysArgGluLysLeuValValArgArgGlyGlnProPheT  
 rpLeuThrLeuHisPheGluGlyArgAsnTyrGlnAlaSerValAspSerLeuThrPheSerValValThrGlyProAlaProSerGlnGluAlaGlyThrLysAlaArgPheProLeuArg  
 30 AspAlaValGluGluGlyAspTrpThrAlaThrValValAspGlnGlnAspCysThrLeuSerLeuGlnLeuThrThrProAlaAsnAlaProIleGlyLeuTyrArgLeuSerLeuGlu  
 AlaSerThrGlyTyrGlnGlySerSerPheValLeuGlyHisPheIleLeuLeuPheAsnAlaTrpCysProAlaAspAlaValTyrLeuAspSerGluGluArgGlnGluTyrValLe  
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 pAsnAsnTyrGlyAspGlyValSerProMetSerTrpIleGlySerValAspIleLeuArgArgTrpLysAsnHisGlyCysGlnArgValLysTyrGlyGlnCysTrpValPheAlaAla  
 35 ValAlaCysThrValLeuArgCysLeuGlyIleProThrArgValValThrAsnTyrAsnSerAlaHisAspGlnAsnSerAsnLeuLeuIleGluTyrPheArgAsnGluPheGlyGluIle  
 eGlnGlyAspLysSerGluMetIleTrpAsnPheHisCysTrpValGluSerTrpMetThrArgProAspLeuGlnProGlyTyrGluGlyTrpGlnAlaLeuAspProThrProGlnGlu  
 LysSerGluGlyThrTyrCysCysGlyProValProValArgAlaIleLysGluGlyAspLeuSerThrLysTyrAspAlaProPheValPheAlaGluValAsnAlaAspValValAspTr  
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 oGluGlySerSerGluGluArgGluAlaPheThrArgAlaAsnHisLeuAsnLysLeuAlaGluLysGluGluThrGlyMetAlaMetArgIleArgValLeuGluSerMetAsnMetGly  
 40 ySerAspPheAspValPheAlaHisIleThrAsnAsnThrAlaAsnThrArgLeuLeuGluCysAlaArgThrValSerTyrAsnGlyIleLeuGlyProGluCysGlyThr  
 LysTyrLeuLeuAsnLeuThrLeuGluProPheSerGluLysSerValProLeuCysIleLeuTyrGluLysTyrArgAspCysLeuThrGluSerAsnLeuIleLysValArgAlaLeuLe  
 uValGluProValIleAsnSerTyrLeuLeuAlaGluArgAspLeuTyrLeuGluAsnProGluIleLysIleArgIleLeuGlyGluProLysGlnLysArgLysLeuValAlaGluValSer  
 LeuGlnAsnProLeuProValAlaLeuGluGlyCysThrPheThrValGluGlyAlaGlyLeuThrGluGluGlnLysThrValGluIleProAspProValGluAlaGlyGluGluValLy  
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 45 ID NO: 2).

(GENBANK ACCESSION NO. BC002829)

GGCAGAGGCTCCCTCACCCCGTCCAGGATGCCAGTCCCCACGACCTCCCACTTCCCACTGTGGCTGGGTGGGCTCAGGG  
 GCTGCCCTTGACCTGGCTAGAGCCCTCCCCAGCTGGTGGTGGAGCTGGCACTCTCTGGGAGGGAGGGGGCTGGGAGGGAATGAG  
 50 TGGGAATGGCAAGAGGCCAGGGTTTGGTGGGATCAGGTTGAGGCAAGTTTGGTTTCTTAAATGCCAAGTTGGGGGCCAGTGGGG  
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 GAGTAAGGGGGAATGAAGGAACCTTCTGCACAAGGAGCTGCCAGCTTTGTGGGGGAGAAAGTGGATGAGGAGGGGCTGAAGAAG  
 CTGATGGGCAGCTGGATGAGAACAGTGACAGCAGGTGGAGTCCAGGAGTATGTGTTTTCTGGCACTCATCTGTCTATGTGC  
 55 AATGACTTCTTCCAGGGCTGCCAGACCCCTGAAGCAGAACTTTGACTTCTGCACTTCTGCACTTCTTGGGCCAGGACTGTTGA  
 TGCCCTTTGAGTTTGTATTCAATAAATTTTTTGTCTGTGAAAAAAGGAAAAAAAAAAAAAAAAAAAA  
 (SEQ ID NO: 3)

Amino acid sequence for S100A2 (GENBANK ACCESSION No. BC002829)

MetMetCysSerSerLeuGluGlnAlaLeuAlaValLeuValThrThrPheHisLysTyrSerCysGlnGluGlyAspLysPheLysLeuSerLysGlyGluMetLysGluLeuLeuHis  
 LysGluLeuProSerPheValGluGluLysValAspGluGlyLeuLysLeuMetGlySerLeuAspGluAsnSerAspGlnGlnValAspPheGlnGluTyrAlaValPheLe  
 60 uAlaLeuIleThrValMetCysAsnAspPheGlnGlyCysProAspArgPro (SEQ ID NO: 4).

(GENBANK ACCESSION NO. NM\_003155)

CAGTTTGCAGAAAGCCAGAGGTGCAAGAACGACGAGCTGCAGCAGCAGCAGCAGCAGCGGCGGTGGCAGCAGCAGCAGCAGCGGC  
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 65 ACCTAAGCTTTCACTGTATCCAGATCCACATCTTCACTCAAGCCAGGAGGGAAGAGGAAAGGGGGGCGAGGAAAAAAGAAAA  
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 (SEQ ID NO: 5)

Amino acid sequence for Stanniocalcin 1 (GENBANK ACCESSION No. NM\_003155)

MetLeuGlnAsnSerAlaValLeuLeuValLeuValIleSerAlaSerAlaThrHisGluAlaGluGlnAsnAspSerValSerProArgLysSerA  
 40 rgValAlaAlaGlnAsnSerAlaGluValValArgCysLeuAsnSerAlaLeuGlnValGlyCysGlyAlaPheAlaCysLeuGluAsnSerThrCy  
 sAspThrAspGlyMetTyrAspIleCysLysSerPheLeuTyrSerAlaAlaLysPheAspThrGlnGlyLysAlaPheValLysGluSerLeuLys  
 CysIleAlaAsnGlyValThrSerLysValPheLeuAlaIleArgArgCysSerPheGlnArgMetIleAlaGluValGlnGluCysTyrS  
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 45 HisIleLeuGlnThrAspHisCysAlaGlnThrHisProArgAlaAspPheAsnArgArgArgThrAsnGluProGlnLysLeuLysValLeuLeuA  
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(GENBANK ACCESSION NO. NM\_001814)

AATTTCTCACCTCTTTTCTCAGCTCCCTGCAGCATGGGTGCTGGGCCCTCCTTGCTGCTCGCCGCCCTCTGCTGCTTCTCTCCGGCG  
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 (SEQ ID NO: 7)

Amino acid sequence for Cathepsin C

(GENBANK ACCESSION No. NM\_001814)

MetGlyAlaGlyProSerLeuLeuLeuAlaAlaLeuLeuLeuLeuSerGlyAspGlyAlaValArgCysAspThrProAlaAsnCysThrTyrL

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 (SEQ ID NO: 9)

35 Amino acid sequence for Myosin X (GENBANK ACCESSION No. NM-012334)

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(GENBANK ACCESSION NO. NM 001743)

(SEO ID NO: 11)

Amino acid sequence for Calmodulin 2 (GENBANK ACCESSION No. NM 001743)

MetAlaAspGlnLeuThrGluGluGlnIleAlaGluPheLysGluAlaPheSerLeuPheAspLysAspGlyAspGlyThrIleThrThrLysGluLeuGlyThrValMetArgSerLeuGlyGlnAsnProThrGluAlaGluLeuGlnAspMetIleAsnGluValAspAlaAspGlyAsnGlyThrIleAspPheProGluPheLeuThrMetMetAlaArgLysMetLysAspThrAspSerGluGluGluIleArgGluAlaPheArgValPheAspLysAspGlyAsnGlyThrIleSerAlaAlaGluLeuArgHisValMetThrAsnLeuGlyGluLysLeuThrAspGluGluValAspGluMetIleArgGluAlaAspIleAspGlyAspGlyGlnValAsnTyrGluGluPheValGlnMetMetThrAlaLys (SEO ID NO: 12).

SEO ID NO, GENBANK ACCESSION NO., Length of oligo, Position of First nucleotide of oligo in target nucleic acid, Sequence of oligo

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20 3871, AI095492,,20,395,AGCATGGGGTAAAGACGAAA,,  
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711

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75 (SEQ ID NO: 4124)



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4692,AI034360,,20,225,ACCAGCTTGGCCTTTTGGC,,  
4693,AI034360,,20,219,TGGCCTTTTGGCAGCTGG,,  
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60 4721,AI034360,,20,51,TTTTTTAAATAATAAGTTCA,,  
4722,AI034360,,20,45,AAATAATAAGTTCAATATGA,,  
4723,AI034360,,20,39,TAAGTTCAATATGAAATAAA,,  
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4727,AI034360,,20,15,TTCTGCTACAACAACCAAAA,,  
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25 4822, AI085559,,20,190,GGCCTCTCCTTATGTGGTGG,,  
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55 4852, AI085559,,20,10,GGACCTATTTTGAGGTTGT,,  
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60 GATGCCATTATCATAGGCCAAGGTCATGAGCTGCTCTGCCATCTCATCGGTGATCTGGCCTCCGAAGGTCAACCATGTTCCAAGTCC  
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5 4870,AI654215,,20,301,AGCAAAGTCTGGATAAGTGAG,,  
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50 4915,AI654215,,20,31,CTGAAAGTGGTACTGGGAAAC,,  
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65 4926,AA505075,,20,135,GCTGCAAGAGGACTCCAGGA,,  
4927,AA505075,,20,129,AGAGGACTCCAGGAGCAAAA,,  
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75 4936,AA505075,,20,75,TTTCATTCAAAAATGCCAACT,,



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4938,AA505075,,20,63,TGCCAACTGGAGAAGTCTGT,,  
4939,AA505075,,20,57,CTGGAGAAGTCTGTTTTTAA,,  
5 4940,AA505075,,20,51,AAGTCTGTTTTTAAATACAT,,  
4941,AA505075,,20,45,GTTTTTAAATACATTTTGT,,  
4942,AA505075,,20,39,AAATACATTTTGTGTATT,,  
4943,AA505075,,20,33,ATTTTGTGTTATTTTAAAA,,  
4944,AA505075,,20,27,TTGTTATTTTAAAAAAAAAA,,  
4945,AA505075,,20,21,TTTTAAAAAAAAAAAAAAAA,,  
10 4946,AA505075,,20,15,AAAAAAAAAAAAAAAAAA,,  
4947,AA505075,,20,9,AAAAAAAAAAAAAAAAAA,,  
4948,AA505075,,20,3,AAAAAAAAAAAAAAAAAA,,  
(GENBANK ACCESSION NO. AA906703)  
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15 ACACGCCTCATGGATTGCTGCCATCAGTTTAACTAATAAAATTTAACTAAAAAGAGGGATGTGAGGGGAGGGGAACTAACGGCAAA  
CTTTTCATGTTTTATCTGGTAAGAAATTTGTGAATTTCTCAGAATTTCCCTGGGCAAAAACCTGTGACCAGAGAATCTGTGAAATAAA  
ATACATAAATCTCTACCCCTTGGAAAAAAAAAAAAAAAAATTTCCAAAAGATGCAGTTACAAGTGTGCTTCTCAGAACAGGAGCATT  
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(SEQ ID NO: 4949)  
20 4950,AA906703,,20,350,AGCCAGAGTATGAAGTGGAA,,  
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4953,AA906703,,20,332,AATGAATGCTCCTGTTCTGA,,  
25 4954,AA906703,,20,326,TGCTCCTGTTCTGAGAAGCA,,  
4955,AA906703,,20,320,TGTTCTGAGAAGCACACTTG,,  
4956,AA906703,,20,314,GAGAAGCACACTTGTAAGT,,  
4957,AA906703,,20,308,CACACTTGTAAGTGCATCTT,,  
4958,AA906703,,20,302,TGTAAGTGCATCTTTTGGAA,,  
30 4959,AA906703,,20,296,TGCATCTTTTGAATTTTTT,,  
4960,AA906703,,20,290,TTTTGGAATTTTTTTTTT,,  
4961,AA906703,,20,284,AATTTTTTTTTTTTTTTC,,  
4962,AA906703,,20,278,TTTTTTTTTTTTTCCAAGGG,,  
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35 4964,AA906703,,20,266,TCCAAGGGTAGAGATTTAT,,  
4965,AA906703,,20,260,GGGTAGAGATTTATGTATTT,,  
4966,AA906703,,20,254,AGATTTATGTATTTATTTTC,,  
4967,AA906703,,20,248,ATGTATTTTATTTACAGAT,,  
4968,AA906703,,20,242,TTTATTTACAGATTTCTCTG,,  
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4971,AA906703,,20,224,TGGTCACAGTTTTTGCCTCA,,  
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4973,AA906703,,20,212,TTTGCCTCAGGAAATTTCTGA,,  
45 4974,AA906703,,20,206,CAGGAAATTTCTGAGAAATT,,  
4975,AA906703,,20,200,AAATCTGAGAAATTCACAAT,,  
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4978,AA906703,,20,182,ATTCTTACCAGATAAAACA,,  
50 4979,AA906703,,20,176,TACCAGATAAAACATGAAAA,,  
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4982,AA906703,,20,158,AAGTTTGCCTTAGTTCCCT,,  
4983,AA906703,,20,152,GCCGTTAGTTCCCTCCCT,,  
55 4984,AA906703,,20,146,AGTTCCCTCCCTCACATC,,  
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4986,AA906703,,20,134,CTCACATCCCTCTTTTAGT,,  
4987,AA906703,,20,128,TCCCTCTTTTAGTTTAAAT,,  
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60 4989,AA906703,,20,116,GTTTTAAATTTATAGTTAAA,,  
4990,AA906703,,20,110,ATTTATAGTTAACTGATG,,  
4991,AA906703,,20,104,TAGTTAACTGATGGCAGCA,,  
4992,AA906703,,20,98,AACTGATGGCAGCAATCCAT,,  
4993,AA906703,,20,92,TGGCAGCAATCCATGAGGCG,,  
65 4994,AA906703,,20,86,CAATCCATGAGGCGTGTCAA,,  
4995,AA906703,,20,80,ATGAGGCGTGTCAAAGAGTG,,  
4996,AA906703,,20,74,CGTGTCAAAGAGTGACATA,,  
4997,AA906703,,20,68,AAAGAGTGACATATGTATG,,  
4998,AA906703,,20,62,TGTACATATGTATGTGTGA,,  
70 4999,AA906703,,20,56,TATGTATGTGTATATTGA,,  
5000,AA906703,,20,50,TGTGTATATTTGAATGCTA,,  
5001,AA906703,,20,44,TATATTGAATGCTAAACATA,,  
5002,AA906703,,20,38,GAATGCTAAACATATTACTG,,  
5003,AA906703,,20,32,TAAACATATTACTGAAAGAC,,  
75 5004,AA906703,,20,26,TATTACTGAAAGACATTT,,

5005,AA906703,,20,20,TGAAAGACACATTTTAATAA,,  
5006,AA906703,,20,14,ACACATTTTAATAAAGATT,,  
5007,AA906703,,20,8,TTTAATAAAGATTCTGTCA,,  
5008,AA906703,,20,2,AAAGATTCTGTCAATTC,,  
5 (GENBANK ACCESSION NO. AI369870)  
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GGGGAGCGGCTGGGATGGCGCGTCCGCGGCCCGCGAGTACAAAGCGGGCGACCTGGTCTTCGCCAAGATGAAGGGCTACCCGCA  
CTGGCCGGCCCGGATTGATGAACTCCAGAGGGCGCTGTGAAGCCTCCAGCAAAACAAGTATCCTATCTTCTTTTGGCAGCCCATGA  
AACTGCATTTCTAGGTCCCAAAGACCTTTTCCATATAAGGAGTACAAAGACAAGTTTGGAAAGTCAAACAAACGGAAAGGATTTA  
10 ACGAAGGATTGTGGGAAATAGAAAATAACCCAGGAGTAAAGTTTACTGGCTACCAGGCAATTCAGCAACAGAGCTCTTCAGAAACT  
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(SEQ ID NO: 5009)  
  
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5011,AI369870,,20,442,CTTGCACTGCACTATTTCC,,  
5012,AI369870,,20,436,TCTGCAGTATTTCCACCTTC,,  
5013,AI369870,,20,430,GTATTTCCACCTTCTCCCTC,,  
5014,AI369870,,20,424,CCACCTTCTCCCTCAGTTTC,,  
5015,AI369870,,20,418,TCCTCCCTCAGTTTCTGAAGA,,  
20 5016,AI369870,,20,412,TCAGTTTCTGAAGAGCTCTG,,  
5017,AI369870,,20,406,TCTGAAGAGCTCTGTTGCTG,,  
5018,AI369870,,20,400,GAGCTCTGTTGCTGAATTGC,,  
5019,AI369870,,20,394,TGTTGCTGAATTGCCTGGTA,,  
5020,AI369870,,20,388,TGAATTGCCTGGTAGCCAGT,,  
25 5021,AI369870,,20,382,GCCTGGTAGCCAGTAACTT,,  
5022,AI369870,,20,376,TAGCCAGTAACTTTACTCC,,  
5023,AI369870,,20,370,GTAACTTTACTCCTGGGTT,,  
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5025,AI369870,,20,358,CCTGGGTTATTTTCTATTTTC,,  
30 5026,AI369870,,20,352,TTATTTTCTATTTCCACAA,,  
5027,AI369870,,20,346,TCTATTTCCCAACAATCCTTC,,  
5028,AI369870,,20,340,TCCCAACAATCCTTCGTTAAA,,  
5029,AI369870,,20,334,ATTCCTTCGTTAAATCCTTT,,  
5030,AI369870,,20,328,TCGTTAAATCCTTTCCGTTT,,  
35 5031,AI369870,,20,322,AATCCTTTCCGTTTGTGTA,,  
5032,AI369870,,20,316,TTCCGTTTGTGACTTTCC,,  
5033,AI369870,,20,310,TTGTTGACTTTCCAAACTT,,  
5034,AI369870,,20,304,GACTTTCCAAACTGTCTTT,,  
5035,AI369870,,20,298,CCAAACTTGTCTTGTACTC,,  
40 5036,AI369870,,20,292,TTGTCCTTGTACTCCTTATA,,  
5037,AI369870,,20,286,TTGTACTCCTTATATGGAAA,,  
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5040,AI369870,,20,268,AAAAGGTCTTTGGGACCTAG,,  
45 5041,AI369870,,20,262,TCTTTGGGACCTAGAAATGC,,  
5042,AI369870,,20,256,GGACCTAGAAATGCAGTTTC,,  
5043,AI369870,,20,250,AGAAATGCAGTTTCATGGGT,,  
5044,AI369870,,20,244,GCAGTTTCATGGGTGCCAAA,,  
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50 5046,AI369870,,20,232,GTGCCAAAAAAGAAGATAGG,,  
5047,AI369870,,20,226,AAAAAGAAGATAGGATACTT,,  
5048,AI369870,,20,220,AAGATAGGATACTTGTGTTGC,,  
5049,AI369870,,20,214,GGATACTTGTGTTGCTGGAGG,,  
5050,AI369870,,20,208,TTGTTTGTGCTGGAGGCTTCAC,,  
55 5051,AI369870,,20,202,GCTGGAGGCTTCACAGCGCC,,  
5052,AI369870,,20,196,GGCTTCACAGCGCCCTCTGG,,  
5053,AI369870,,20,190,ACAGCGCCCTCTGGGAGTTC,,  
5054,AI369870,,20,184,CCCTCTGGGAGTTCATCAAT,,  
5055,AI369870,,20,178,GGGAGTTTCATCAATCCGGGC,,  
60 5056,AI369870,,20,172,TCATCAATCCGGGCCGGCCA,,  
5057,AI369870,,20,166,ATCCGGGCCGGCCAGTGCGG,,  
5058,AI369870,,20,160,GCCGGCCAGTGCGGGTAGCC,,  
5059,AI369870,,20,154,CAGTGCGGGTAGCCCTTCAT,,  
5060,AI369870,,20,148,GGGTAGCCCTTCATCTTGGC,,  
65 5061,AI369870,,20,142,CCCTTCATCTTGGCGAAGAC,,  
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5063,AI369870,,20,130,GCGAAGACCAAGTCCGCCGC,,  
5064,AI369870,,20,124,ACCAGGTCGCCCGCTTTGTA,,  
5065,AI369870,,20,118,TCGCCCCCTTTGTACTCGCG,,  
70 5066,AI369870,,20,112,GCTTTGTACTCGCGGGGCCG,,  
5067,AI369870,,20,106,TACTCGCGGGGCCGCGGACG,,  
5068,AI369870,,20,100,CGGGGCCGCGGACGCGCCAT,,  
5069,AI369870,,20,94,CGCGGACGCGCCATCCAGC,,  
5070,AI369870,,20,88,CGCGCCATCCAGCCGCTCC,,  
75 5071,AI369870,,20,82,ATCCAGCCGCTCCCTTCC,,

5072,AI369870,,20,76,GCCGCTCCCCTTCCTGGTAG,,  
5073,AI369870,,20,70,CCCCCTCCTGGTAGTCCTTG,,  
5074,AI369870,,20,64,CCTGGTAGTCCTTGGTCGCC,,  
5075,AI369870,,20,58,AGTCCTTGGTCGCCGCGAAG,,  
5 5076,AI369870,,20,52,GGTCGCCGCGAAGATGCCG,,  
5077,AI369870,,20,46,CCGCGAAGATGCCGGGAGGC,,  
5078,AI369870,,20,40,AGATGCCGGGAGGCCGCCGCC,,  
5079,AI369870,,20,34,CGGGAGGCCGCCGCCGCCGCC,,  
5080,AI369870,,20,28,GCCGCCGCCGCCGCCGCCGA,,  
10 5081,AI369870,,20,22,CCCCCGGGGCCGACGAATT,,  
5082,AI369870,,20,16,CGGGCCGACGAATTGCCGCC,,  
5083,AI369870,,20,10,GACGAATTGCCGCCGCTCC,,  
5084,AI369870,,20,4,TTGCCGCCGCTCCCCGCCG,,  
(GENBANK ACCESSION NO. AA463249)  
15 TTTTTTTTTTTTTTTTTTCTCAAGAAAAAAGTTTAATAGCAAGGAGTTTCCATCAGTCCCGGTCTTTGTGAGGATTACCACAACA  
AACACTTAAAAAGGATACAACAGGTACTTATTAATGCTGCCTTGCCCTTTACCTCTTCTTTTTTTTTTTTGTAGATGGAGTCTCG  
CTCTGCTGCCAGCCTGAAGTGCAGTGGTGTGATCTCGGCTCACTGCAACCTCCGCTTCCAGGTTTAGGTGATTCTCTTGCCTCGGC  
CTCCCGAGTAGCTGGGATGGACTACAGGCACATGTACCATGCCAGCTAATTTTTTGTATTTTAGTA  
(SEQ ID NO: 5085)  
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5089,AA463249,,20,297,TTAGCTGGGCATGGTGACAT,,  
25 5090,AA463249,,20,291,GGGCATGGTGACATGTGCCT,,  
5091,AA463249,,20,285,GGTGACATGTGCCTGTAGTC,,  
5092,AA463249,,20,279,ATGTGCCTGTAGTCCATCCC,,  
5093,AA463249,,20,273,CTGTAGTCCATCCCAGCTAC,,  
5094,AA463249,,20,267,TCCATCCCAGCTACTCGGGA,,  
30 5095,AA463249,,20,261,CCAGCTACTCGGGAGGCCGA,,  
5096,AA463249,,20,255,ACTCGGGAGGCCGAGGCAAG,,  
5097,AA463249,,20,249,GAGGCCGAGGCAAGAGAATC,,  
5098,AA463249,,20,243,GAGGCAAGAGAATCACCTAA,,  
5099,AA463249,,20,237,AGAGAATCACCTAAACCTGG,,  
35 5100,AA463249,,20,231,TCACCTAAACCTGGAAGGCG,,  
5101,AA463249,,20,225,AAACCTGGAAGGCGGAGGTT,,  
5102,AA463249,,20,219,GGAAGGCGGAGGTTGCAGTG,,  
5103,AA463249,,20,213,CGGAGGTTGCAGTGAGCCGA,,  
5104,AA463249,,20,207,TTGCAGTGAGCCGAGATCAC,,  
40 5105,AA463249,,20,201,TGAGCCGAGATCACACCACT,,  
5106,AA463249,,20,195,GAGATCACACCACTGCACTT,,  
5107,AA463249,,20,189,ACACCACTGCACTTCAGGCT,,  
5108,AA463249,,20,183,CTGCACTTCAGGCTGGGCAG,,  
5109,AA463249,,20,177,TCAGGCTGGGCAGCAGAGC,,  
45 5110,AA463249,,20,171,CTGGGCAGCAGAGCGAGACT,,  
5111,AA463249,,20,165,AGCAGAGCGAGACTCCATCT,,  
5112,AA463249,,20,159,GCGAGACTCCATCTCAAAAA,,  
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50 5115,AA463249,,20,141,AAAAAAGGAAGAGAG,,  
5116,AA463249,,20,135,AAAAAAGGAAGAGGTAAAA,,  
5117,AA463249,,20,129,AGGAAGAGGTAAAGGCAAG,,  
5118,AA463249,,20,123,AGGTAAAGGCAAGGCAGCA,,  
5119,AA463249,,20,117,AAGGCAAGGCAGCATTTAAT,,  
55 5120,AA463249,,20,111,AGGCAGCATTTAATAAGTAC,,  
5121,AA463249,,20,105,CATTTAATAAGTACCTGTTG,,  
5122,AA463249,,20,99,ATAAGTACCTGTTGTATCCT,,  
5123,AA463249,,20,93,ACCTGTTGTATCCTTTTAAG,,  
5124,AA463249,,20,87,TGTATCCTTTTAAGTGTG,,  
60 5125,AA463249,,20,81,CTTTTAAGTGTGTTGTG,,  
5126,AA463249,,20,75,AGTGTGTTGTGTTGTAATCC,,  
5127,AA463249,,20,69,TGTTGTGTTAATCTCACAA,,  
5128,AA463249,,20,63,GGTAATCCTCACAAAGACCG,,  
5129,AA463249,,20,57,CCTCACAAAGACCGGACTG,,  
65 5130,AA463249,,20,51,AAAGACCGGACTGATGGAA,,  
5131,AA463249,,20,45,CGGGACTGATGGAACTCCT,,  
5132,AA463249,,20,39,TGATGGAACTCCTTGCTAT,,  
5133,AA463249,,20,33,AAACTCCTTGCTATTAACT,,  
5134,AA463249,,20,27,CTTGCTATTAACTTTTTT,,  
70 5135,AA463249,,20,21,ATTAACTTTTTTCTTGAG,,  
5136,AA463249,,20,15,CTTTTTTCTTGAGGAAAAA,,  
5137,AA463249,,20,9,TTCTTGAGGAAAAA,,  
5138,AA463249,,20,3,AGGAAAAA,,  
(GENBANK ACCESSION NO. R38894)

TTTTTTACAGCATAGCGGTTTATTCATGCCATCATAAGTCGATCTGTATTCTTCAAGTACATTTTGAATTTATAATGAAGACAGTTT  
AAGGCATAACTCTTCCCCTCAAATCTATGGTCTTCTCAAGTGAGACACTAGAGAGAGTAGAANGGGAGGNTGAGATAGGGC  
(SEQ ID NO: 5139)

- 5 5140,R38894,,20,152,GCCCTATCTCANCCTCCCNCT,,  
5141,R38894,,20,146,TCTCANCCTCCCNCTTCTACT,,  
5142,R38894,,20,140,CCTCCCNCTTCTACTCTCTCT,,  
5143,R38894,,20,134,NTTCTACTCTCTCTAGTGTC,,  
5144,R38894,,20,128,CTCTCTCTAGTGCTCACTT,,  
10 5145,R38894,,20,122,CTAGTGCTCACTTGAGAAA,,  
5146,R38894,,20,116,TCTCACTTGAGAAAGACCAT,,  
5147,R38894,,20,110,TTGAGAAAGACCATAGATTT,,  
5148,R38894,,20,104,AAGACCATAGATTTGAGTGG,,  
5149,R38894,,20,98,ATAGATTTGAGTGGGAAGAG,,  
15 5150,R38894,,20,92,TTGAGTGGGAAGAGTTATGC,,  
5151,R38894,,20,86,GGGAAGAGTTATGCCTTAAA,,  
5152,R38894,,20,80,AGTTATGCCTTAAACTGTCT,,  
5153,R38894,,20,74,GCCTTAAACTGTCTTCATTA,,  
5154,R38894,,20,68,AACTGTCTTCATTATAAAAT,,  
20 5155,R38894,,20,62,CTTCATTATAAAATCAAAAT,,  
5156,R38894,,20,56,TATAAAATCAAAATGTACTT,,  
5157,R38894,,20,50,TTCAAATGTACTTGAAGAA,,  
5158,R38894,,20,44,ATGTACTTGAAGAATACAGA,,  
5159,R38894,,20,38,TTGAAGAATACAGATCGACT,,  
25 5160,R38894,,20,32,AATACAGATCGACTGTATGA,,  
5161,R38894,,20,26,GATCGACTGTATGATGGCAT,,  
5162,R38894,,20,20,CTGTATGATGGCATGAATAA,,  
5163,R38894,,20,14,GATGGCATGAATAAACCGCT,,  
5164,R38894,,20,8,ATGAATAAACCGCTATGCTG,,  
30 5165,R38894,,20,2,AAACCGCTATGCTGTAAAAA,,  
(GENBANK ACCESSION NO. R49144)  
TTTTTTTTTTTTTGGAGATGACCTGNACTTTTAAATGGCACAGCCCCAGCTCCAGCAAAGCAGCAAGACAGGAAGCTATGCAAAGC  
TGCTCAGAGGTGCAAGTGGCCAAACAACCTCTAGGAGATCGCCTGTNTTCCCTCCCATCCCCAAGCTTATGACGTGGCTCCATGCCCCA  
GGGAACCTTTGGGCCANCCCANCCCCANTCCCAAACCTCATAATNCACAGAGGGAGCCTGGGCCAAG  
35 (SEQ ID NO: 5166)
- 5167,R49144,,20,222,CTTGGCCCAGGCTCCCTCTG,,  
5168,R49144,,20,216,CCAGGCTCCCTCTGTGNATT,,  
5169,R49144,,20,210,TCCCTCTGTGNATTATGAGG,,  
40 5170,R49144,,20,204,TGTGNATTATGAGGGTTTGG,,  
5171,R49144,,20,198,TTATGAGGGTTTGGGANTGG,,  
5172,R49144,,20,192,GGGTTTGGGANTGGGNTGG,,  
5173,R49144,,20,186,GGGANTGGGNTGGGNTGGC,,  
5174,R49144,,20,180,GGGNTGGGNTGGCCAAAG,,  
45 5175,R49144,,20,174,GGGNTGGCCAAAGTTCCCT,,  
5176,R49144,,20,168,GCCCAAAGTTCCCTGGGCAT,,  
5177,R49144,,20,162,AGTTCCCTGGGCATGGAGCC,,  
5178,R49144,,20,156,CTGGGCATGGAGCCACGTCA,,  
5179,R49144,,20,150,ATGGAGCCACGTCAAGCT,,  
50 5180,R49144,,20,144,CCACGTCATAAGCTTGGGGG,,  
5181,R49144,,20,138,CATAAGCTTGGGGATGGGA,,  
5182,R49144,,20,132,CTTGGGGATGGGAGGGAAN,,  
5183,R49144,,20,126,GGATGGGAGGGAANACAGGC,,  
5184,R49144,,20,120,GAGGGAANACAGGCGATCTC,,  
55 5185,R49144,,20,114,ANACAGGCGATCTCTAGAG,,  
5186,R49144,,20,108,GCGATCTCTAGAGTTGTTT,,  
5187,R49144,,20,102,TCCTAGAGTTGTTTGGCCAC,,  
5188,R49144,,20,96,AGTTGTTTGGCCACTGCACC,,  
5189,R49144,,20,90,TTGGCCACTGCACCTCTGAG,,  
60 5190,R49144,,20,84,ACTGCACCTCTGAGCAGCTT,,  
5191,R49144,,20,78,CCTCTGAGCAGCTTTGCATA,,  
5192,R49144,,20,72,AGCAGCTTTGCATAGCTTCC,,  
5193,R49144,,20,66,TTGCATAGCTTCTGTCTT,,  
5194,R49144,,20,60,TAGCTTCTGTCTTGTGCTGCT,,  
65 5195,R49144,,20,54,CCTGTCTTGTGCTTTGTCTG,,  
5196,R49144,,20,48,TTGCTGCTTTGTGAGGCTG,,  
5197,R49144,,20,42,CTTTGCTGGAGCTGGGGCTG,,  
5198,R49144,,20,36,TGGAGCTGGGGCTGTGCCAT,,  
5199,R49144,,20,30,TGGGGCTGTGCCATTAAAAAG,,  
70 5200,R49144,,20,24,TGTGCCATTAAAAAGTNCAGG,,  
5201,R49144,,20,18,ATTAAAAAGTNCAGGTCACTT,,  
5202,R49144,,20,12,AGTNCAGGTCACTCCAAAAA,,  
5203,R49144,,20,6,GGTCACTCCAAAAAATAA,,  
(GENBANK ACCESSION NO. AA398883)

TATGTCTACTATTTTATTGATGATGTGTTTATAGAATCACAAAATTTAGAAACATAAGAAGGATTAGGTATCACCTAAATTCAAAG  
AAATGTGTGTTTCTAGGTTGCTAAATTCAGAGAAAAGTATGATTTGGTTTGGTTCAATTTAAACAGGTACAAAACAGAATTATATT  
TCAAATTTAGAAGATACGGTATTAAGTGATTTCATCTTATTTTGGACATTTTCTCAAGGAGAAATTTTCTGGAAGAAAAAGTACATT  
TATATGTGGGCTTATTAAGAGAAAAGAGAGAAAAGGCATGCTATTTAATCATTAAATTCCTTGATGATGACGATCATCAAGATGAG  
5 AAAGAAAAGAAAATATGAGCCCAAGAGAATCTGTGTGGCCAGCAATCAGTTTACCAGAACAATCTGCAAGGTGAACATTTTCCAAATGG  
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(SEQ ID NO: 5204)

10 5205,AA398883,,20,514,TCCATGTATCACCCCTTCCTA,,  
5206,AA398883,,20,508,TATCACCCCTTCCTATCTACA,,  
5207,AA398883,,20,502,CCTTCCTATCTACATAAGCA,,  
5208,AA398883,,20,496,TATCTACATAAGCAAAATAA,,  
5209,AA398883,,20,490,CATAAGCAAAATAAGCCAC,,  
15 5210,AA398883,,20,484,CAAAATAAGCCACAGCATC,,  
5211,AA398883,,20,478,AAGCCACAGCATCCTCTCT,,  
5212,AA398883,,20,472,ACAGCATCCTCTCTATGGCA,,  
5213,AA398883,,20,466,TCCTCTCTATGGCAGATTCT,,  
5214,AA398883,,20,460,CTATGGCAGATTCTCATCCC,,  
20 5215,AA398883,,20,454,CAGATTCTCATCCCCGTAGA,,  
5216,AA398883,,20,448,CTCATCCCCGTAGATGCAAT,,  
5217,AA398883,,20,442,CCCGTAGATGCAATTAGTCT,,  
5218,AA398883,,20,436,GATGCAATTAGTCTGTCACT,,  
5219,AA398883,,20,430,ATTAGTCTGTCACTCCATTT,,  
25 5220,AA398883,,20,424,CTGTCACTCCATTTGGAAAA,,  
5221,AA398883,,20,418,CTCCATTTGGAAAAATGTTCA,,  
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35 5230,AA398883,,20,364,CAACAGATTCTCTGGCTCA,,  
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5252,AA398883,,20,232,TCTTCCAGAAAAATCTCTCT,,  
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60 5255,AA398883,,20,214,CTTGAGGAAAAATGTCCAAA,,  
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5257,AA398883,,20,202,TGTCCAAAAATAAGATGAATC,,  
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5259,AA398883,,20,190,GATGAATCACTTAATACCGT,,  
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70 5265,AA398883,,20,154,ATATAATTCTGTTTGAGACC,,  
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75 5270,AA398883,,20,124,GAACCAACCAAAATCACT,,

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10 5280,AA398883,,20,64,GAATTTAGGTGATACCTAAA,,  
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5287,AA398883,,20,22,TGTGATTCTATAAAACACAT,,  
5288,AA398883,,20,16,TCTATAAAACACATCATCAA,,  
5289,AA398883,,20,10,AAACACATCATCAATAAAAT,,  
20 5290,AA398883,,20,4,ATCATCAATAAAATAGTGAC,,  
(GENBANK ACCESSION NO. AA425700)  
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TTACTTTTAAAGAAATGATACATTTGTGGAAAAATGTATCAAAATAGAGCTTTAGGCTAAGGGCAGTAAATTTGGCATGACTAAG  
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25 CAGTAAGGATGTTCTTCTCTTCTGGAACAGAAGGGGCACCTTTCTCATGGGAAATTGATTACCTGCTTTTAGGGAGACAGCAGGTCA  
GGGAACCCCTTCCTG  
(SEQ ID NO: 5291)

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5295,AA425700,,20,325,CTGCTGTCTCCCTAAAAGCA,,  
5296,AA425700,,20,319,TCTCCCTAAAAGCAGGTAAT,,  
5297,AA425700,,20,313,TAAAAGCAGGTAATACAATT,,  
35 5298,AA425700,,20,307,CAGGTAATACAATTCCCAT,,  
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45 5308,AA425700,,20,247,TACTGGAGACTGGGAGTAGA,,  
5309,AA425700,,20,241,AGACTGGGAGTAGATGACGA,,  
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5312,AA425700,,20,223,GAATGGATCTGTACAAACA,,  
50 5313,AA425700,,20,217,GATCTGTACAAACAAATCTA,,  
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60 5323,AA425700,,20,157,TTCTTAGTCATGCCACAATT,,  
5324,AA425700,,20,151,GTATGCCACAATTTACTGC,,  
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70 5333,AA425700,,20,97,CACAAATGTATCATTTCTTT,,  
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5337,AA425700,,20,73,AGTAAATAAGCTCTTGATCC,,  
75 5338,AA425700,,20,67,TAAGCTCTTGATCCCAACTG,,



5339,AA425700,,20,61,CTTGATCCCAACTGTTCTTT,,  
5340,AA425700,,20,55,CCCAACTGTTCTTTGGGTCT,,  
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5 5343,AA425700,,20,37,CTCTATTCTCCATATGAGGG,,  
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5345,AA425700,,20,25,TATGAGGGTCCCTTGATTCT,,  
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10 5348,AA425700,,20,7,TCAAATAAAAGATTAAATAA,,  
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(GENBANK ACCESSION NO. AA459692)  
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15 CAAAGCAAAGGAGAGAAACAAGAGTATCCTGAGGCGGTCTCTGCGAGTGCTCATAGCTGTTCTCTTACGCTTCCACCTGGTGGCC  
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(SEQ ID NO: 5350)

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5354,AA459692,,20,249,AGTCCAGGGCCACCAGGTGG,,  
5355,AA459692,,20,243,GGGCCACCAGGTGGAAGGCT,,  
5356,AA459692,,20,237,CCAGGTGGAAGGCTAAGGAG,,  
25 5357,AA459692,,20,231,GGAAGGCTAAGGAGGAACAG,,  
5358,AA459692,,20,225,CTAAGGAGGAACAGCTATGA,,  
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5366,AA459692,,20,177,CTTGTCTCTCCTCTTGCTT,,  
35 5367,AA459692,,20,171,CTCTCCTCTTGCTTTGCTGT,,  
5368,AA459692,,20,165,TCTTGCTTTGCTGTTTTGT,,  
5369,AA459692,,20,159,TTTGCTGTTTTGTTCTCCA,,  
5370,AA459692,,20,153,GTITTTGTTCTCAAATGAC,,  
5371,AA459692,,20,147,GTITCTCAAATGACCATCAT,,  
40 5372,AA459692,,20,141,CAAAATGACCATCATCGTCAG,,  
5373,AA459692,,20,135,ACCATCATCGTCAGAAGACA,,  
5374,AA459692,,20,129,ATCGTCAGAAGACAATTTTG,,  
5375,AA459692,,20,123,AGAAGACAATTTTGACCAG,,  
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45 5377,AA459692,,20,111,TGACCACGAAATGTTGTAG,,  
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5379,AA459692,,20,99,GTITGTAGTGAGAATATCAG,,  
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50 5382,AA459692,,20,81,AAGCAGGTGTCTGATATTCC,,  
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55 5387,AA459692,,20,51,GTITATTCCAGGCAGGTTTA,,  
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5389,AA459692,,20,39,CAGGTTTATGTTTCTTGCT,,  
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5391,AA459692,,20,27,TCCTTGCTAATACACGTACA,,  
60 5392,AA459692,,20,21,CTAATACACGTACAATTTTA,,  
5393,AA459692,,20,15,CACGTACAATTTTACAATA,,  
5394,AA459692,,20,9,CAATTTTACAATACTGTAT,,  
5395,AA459692,,20,3,TACAATACTGTATTAAACAG,,  
(GENBANK ACCESSION NO. AA487557)  
65 TTTTCAAATTTTAATTAATAATCTTTATTGAATAAAAAATGTTTCAGACTAGGTAAGACTAAGAAAGCAGAATGTTTACATCTCTAAA  
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70 (SEQ ID NO: 5396)

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75 5400,AA487557,,20,320,CACTAATTTTAAATACTTA,,

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5403,AA487557,,20,302,TACTAGCTCTGAAATATATT,,  
5404,AA487557,,20,296,CTCTGAAATATATTGATTTT,,  
5 5405,AA487557,,20,290,AATATATTGATTTTATCAC,,  
5406,AA487557,,20,284,TTGATTTTATCACAGTATT,,  
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10 5410,AA487557,,20,260,GGGTGAAATTAACCAACTA,,  
5411,AA487557,,20,254,AATTAACCAACTATAGGCC,,  
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5416,AA487557,,20,224,GATGATTTTCTAGTCTTAAG,,  
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5421,AA487557,,20,194,ATTATAAACTTGAGTACATT,,  
5422,AA487557,,20,188,AACTTGAGTACATTTGTTGT,,  
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5424,AA487557,,20,176,TTTGTGTACACAGTTGATA,,  
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35 5435,AA487557,,20,110,TTTCTTTGTACTGCAATTA,,  
5436,AA487557,,20,104,TTGTACTGCATTTATAGAGA,,  
5437,AA487557,,20,98,TGCAATTTATAGAGATTAGC,,  
5438,AA487557,,20,92,TATAGAGATTTAGCTTTAAT,,  
5439,AA487557,,20,86,GATTTAGCTTTAATATTTTT,,  
40 5440,AA487557,,20,80,GCTTTAATATTTTTAGAGA,,  
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5447,AA487557,,20,38,GTCTTACCTAGTCTGAAACA,,  
5448,AA487557,,20,32,CCTAGTCTGAAACATTTTAA,,  
5449,AA487557,,20,26,CTGAAACATTTTATTTCAAT,,  
50 5450,AA487557,,20,20,CATTTTTATTTCAATAAAGAT,,  
5451,AA487557,,20,14,TATTTCAATAAAGATTTTAAT,,  
5452,AA487557,,20,8,ATAAAGATTTTAATTAATAAAT,,  
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(GENBANK ACCESSION NO. T69168)  
55 CAATAANGTGCNTTTCAACTCAGCAATATACATATCANTGCNTTTCCTCATTANTTAATTGATCCATCAATAAATATACAAAAACCA  
GAGGAAGGGTGTGCTCTGAAAAGTCAAAGTAAACAATAACAGTGGTCATTGTACAGCACAAAGANTGAACAATGGGCTATTCTTTGAA  
AACTCAAAAACAAATGATTTACACAAAGACATATCTATAACATAAAGGTGAATGGACCATGTTATTCTTATTCTTANGTACATTTTGC  
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5457,T69168,,20,314,GTAGCCAACATTCAATCAAN,,  
5458,T69168,,20,308,AACATTCATTCAANACTGNA,,  
65 5459,T69168,,20,302,CATTCAANACTGNAATATCA,,  
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5461,T69168,,20,290,NAATATCAGAGGAGTAAGGA,,  
5462,T69168,,20,284,CAGAGGAGTAAGGAGAGAGG,,  
5463,T69168,,20,278,AGTAAGGAGAGAGGAAACAT,,  
70 5464,T69168,,20,272,GAGAGAGGAAACATTGACT,,  
5465,T69168,,20,266,GGAAACATTTGACTTANCTG,,  
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5467,T69168,,20,254,CTTANCTGGAAAAGCAAAAT,,  
5468,T69168,,20,248,TGAAAAGCAAAATGTACNT,,  
75 5469,T69168,,20,242,AGCAAAATGTACNTAAGAAT,,

5470,T69168,,20,236,ATGTACNTAAGAATAAGAAT,,  
5471,T69168,,20,230,NTAAGAATAAGAATAACATG,,  
5472,T69168,,20,224,ATAAGAATAACATGGTCCAT,,  
5473,T69168,,20,218,ATAACATGGTCCATTACACCT,,  
5 5474,T69168,,20,212,TGGTCCATTACCTTTATGT,,  
5475,T69168,,20,206,ATTACCTTTATGTTATAGA,,  
5476,T69168,,20,200,CTTTATGTTATAGATATGTC,,  
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5491,T69168,,20,110,ACTGTTATTGTTACTTTGAC,,  
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25 5494,T69168,,20,92,ACTTTTCAGAGCACACCCCTT,,  
5495,T69168,,20,86,CAGAGCACACCCCTTCCTCTG,,  
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30 5499,T69168,,20,62,TTGTATATTTATTTGATGGAT,,  
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5501,T69168,,20,50,TGATGGATCAATTAANTAAT,,  
5502,T69168,,20,44,ATCAATTAANTAATGAGGAA,,  
5503,T69168,,20,38,TAANTAATGAGGAAANGCAN,,  
35 5504,T69168,,20,32,ATGAGGAAANGCANTGATAT,,  
5505,T69168,,20,26,AAANGCANTGATATGTATAT,,  
5506,T69168,,20,20,ANTGATATGTATATTGCTGA,,  
5507,T69168,,20,14,ATGTATATTGCTGAGTTGAA,,  
5508,T69168,,20,8,ATTGCTGAGTTGAAANGCAC,,  
40 5509,T69168,,20,2,GAGTTGAAANGCACNTTATT,,  
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45 AGGAAGGTGCCCAGAATACCAATGTCTCCTGCCTTAACACATTAATACAAAGTTTGCCAATTGTTTTGAATTTCCAAATGTATTCC  
TGAAAAAAGAAAGAACTTAAACACTATATTATAGACATATGTTAGAAAGTCTAGAAATGCACCCAAATTCCTTCCATTCTACTTT  
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(SEQ ID NO: 5510)  
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5 5814,AA293300,,20,56,TTATGTGGTTTTTATACATT,,  
5815,AA293300,,20,50,GGTTTTTATACATTTTTTAA,,  
5816,AA293300,,20,44,TATACATTTTTTAATAAGAT,,  
5817,AA293300,,20,38,TTTTTAATAAGATGCACCT,,  
5818,AA293300,,20,32,AATAAGATGCATTTATGTC,,  
10 5819,AA293300,,20,26,ATGCATTTATGTCATTTTT,,  
5820,AA293300,,20,20,TTTATGTCATTTTTTAATAA,,  
5821,AA293300,,20,14,TCATTTTTTAATAAAGTCTG,,  
5822,AA293300,,20,8,TTAATAAAGTCTGAAGAAT,,  
5823,AA293300,,20,2,AAAGTCTGAAGAATTAAGT,,  
15 (GENBANK ACCESSION NO. AA278764)  
TTTTTTTTTTTTTTTTTTTGACAGGAAGTGTTTTATTCCAACCACTCACCTCCTTAGAATGGGAGGCGAACAGTGAAATAGTGCA  
TTTATCTTAAAGTGAAATAATCCAGGATGGTAGGGCGAGACCCTGTGATGGGTGAATTTACCTCACTTGATACCAAGGGCCCTTA  
ATACTCGGGGAAGTGGGACTTTGTGCGACAAAGCCAGGACAATCCCCCTACCCCCACCCAGCAGTGATTAAAAACCCGTACG  
GTCACTTCTATGTGATGGCTGTCTCCCTCTCACCAGACTGCATAGCGGTTGCAGATGAACATTTGGCACCTAGATGGGGGTCAAGG  
20 AGCTGGGGCTGTGATTAGGGAAGATGCTGAGGGGGACTGGGAGTCTCTGTTTGAATCTTGAAGCAAGGGGTGA  
(SEQ ID NO: 5824)

5825,AA278764,,20,404,TCACCCCTTGCTTCAAGATT,,  
5826,AA278764,,20,398,CTTGCTTCAAGATTCAAACA,,  
25 5827,AA278764,,20,392,TCAAGATTCAAACAGAGACT,,  
5828,AA278764,,20,386,TTCAAACAGAGACTCCCACT,,  
5829,AA278764,,20,380,CAGAGACTCCCACTCCCTCT,,  
5830,AA278764,,20,374,CTCCCACTCCCTCAGCAT,,  
5831,AA278764,,20,368,GTCCCCCTCAGCATCTTCCC,,  
30 5832,AA278764,,20,362,CTCAGCATCTTCCCTGAATC,,  
5833,AA278764,,20,356,ATCTTCCCTGAATCACAGCC,,  
5834,AA278764,,20,350,CCTGAATCACAGCCCCAGCT,,  
5835,AA278764,,20,344,TCACAGCCCCAGCTCCTTGA,,  
5836,AA278764,,20,338,CCCCAGCTCCTTGACCCCCA,,  
35 5837,AA278764,,20,332,CTCCTTGACCCCCATCTAGG,,  
5838,AA278764,,20,326,GACCCCCATCTAGGTGCCAA,,  
5839,AA278764,,20,320,CATCTAGGTGCCAAATGTTT,,  
5840,AA278764,,20,314,GGTGCCAAATGTTTCTCTGC,,  
5841,AA278764,,20,308,AAATGTTTCTCTGCAACCGC,,  
40 5842,AA278764,,20,302,TCATCTGCAACCGCTATGCA,,  
5843,AA278764,,20,296,GCAACCGCTATGCAGTCTGG,,  
5844,AA278764,,20,290,GCTATGCAGTCTGGTGAGAG,,  
5845,AA278764,,20,284,CAGTCTGGTGAGAGGGAGAC,,  
5846,AA278764,,20,278,GGTGAGAGGGAGACAGCCAT,,  
45 5847,AA278764,,20,272,AGGGAGACAGCCATCACATA,,  
5848,AA278764,,20,266,ACAGCCATCACATAGAAAGT,,  
5849,AA278764,,20,260,ATCACATAGAAAGTGACCGT,,  
5850,AA278764,,20,254,TAGAAAGTGACCGTACGGGT,,  
5851,AA278764,,20,248,GTGACCGTACGGGTTTTTAA,,  
50 5852,AA278764,,20,242,GTACGGGTTTTTAATCACTG,,  
5853,AA278764,,20,236,GTTTTTAATCACTGCTGGGT,,  
5854,AA278764,,20,230,AATCACTGCTGGGTGGGGTG,,  
5855,AA278764,,20,224,TGCTGGGTGGGGTGGGGGTA,,  
5856,AA278764,,20,218,GTGGGGTGGGGGTAGGGGGA,,  
55 5857,AA278764,,20,212,TGGGGGTAGGGGGATTGTCC,,  
5858,AA278764,,20,206,TAGGGGGATTGTCTGGCTT,,  
5859,AA278764,,20,200,GATTGTCTGGCTTTGTCTGA,,  
5860,AA278764,,20,194,CCTGGCTTTGTGCAAAAGT,,  
5861,AA278764,,20,188,TTTGTGCAAAAGTCCCACT,,  
60 5862,AA278764,,20,182,GACAAAGTCCCACTTCCCG,,  
5863,AA278764,,20,176,GTCCCACTTCCCGAGTATT,,  
5864,AA278764,,20,170,CTTCCCGAGTATTAAGGGC,,  
5865,AA278764,,20,164,CGAGTATTAAGGGCCCTTGG,,  
5866,AA278764,,20,158,TTAAGGGCCCTTGGTATCAA,,  
65 5867,AA278764,,20,152,GCCCTTGGTATCAAGTGAGG,,  
5868,AA278764,,20,146,GGTATCAAGTGAGGTAATTA,,  
5869,AA278764,,20,140,AAGTGAGGTAATTCACCCA,,  
5870,AA278764,,20,134,GGTAAATTCACCCATCACAG,,  
5871,AA278764,,20,128,TTACCCATCACAGGGTCTC,,  
70 5872,AA278764,,20,122,CATCACAGGGTCTCGCCCTA,,  
5873,AA278764,,20,116,AGGGTCTCGCCCTACCATCC,,  
5874,AA278764,,20,110,TCGCCCTACCATCCTGGAAT,,  
5875,AA278764,,20,104,TACCATCCTGGAATTATTTT,,  
5876,AA278764,,20,98,CCTGGAATTATTTCACTTTT,,  
75 5877,AA278764,,20,92,ATTATTTCACTTTTAAGATA,,

5878,AA278764,,20,86,TCACTTTTAAGATAAATGCA,,  
5879,AA278764,,20,80,TTAAGATAAATGCACTATTT,,  
5880,AA278764,,20,74,TAAATGCACTATTTCACTGT,,  
5881,AA278764,,20,68,CACTATTTCACTGTTCCGCT,,  
5 5882,AA278764,,20,62,TTCACTGTTCCGCTCCCAT,,  
5883,AA278764,,20,56,GTTCGCTCCCATTTCTAAGG,,  
5884,AA278764,,20,50,CTCCCATTTCTAAGGAGGTGA,,  
5885,AA278764,,20,44,TTCTAAGGAGGTGAGGTGGT,,  
5886,AA278764,,20,38,GGAGGTGAGGTGGTGGAAAT,,  
10 5887,AA278764,,20,32,GAGGTGGTTGGAATAAAAAAC,,  
5888,AA278764,,20,26,GTGGAATAAAAAACAGTTCC,,  
5889,AA278764,,20,20,ATAAAAAACAGTTCTGTCAA,,  
5890,AA278764,,20,14,ACAGTTCTGTCAAAAAA,,  
5891,AA278764,,20,8,CCTGTCAAAAAA,,  
15 5892,AA278764,,20,2,AAAAAAAAAAAAAAAA,,  
(GENBANK ACCESSION NO. AA678160)  
ACCAATCTTAATTAGCAATTTTTTAATGGGGCCACAGTCTTTTCTCTATTATTGTAAATGTTTCTTTTTTAAAGATTTGCCCTAGT  
ACAATCCAAGTCCGCTTCCAAATAAAGTAAAGTATTAGTATGAAAAACCCTGGCTACAATAAATTAGAGACCATTTAATCCTGC  
AATCTTGGTCAAGTTCATATTTCCACCATAGCACATTAG  
20 (SEQ ID NO: 5893)

5894,AA678160,,20,195,CTAATGTGCTATGGTGGAAA,,  
5895,AA678160,,20,189,TGCTATGGTGGAAATATGAA,,  
5896,AA678160,,20,183,GGTGGAAATATGAACCTTGAC,,  
25 5897,AA678160,,20,177,AATATGAACCTTGACCAAGAT,,  
5898,AA678160,,20,171,AACCTGACCAAGATTGCAGG,,  
5899,AA678160,,20,165,ACCAAGATTGCAGGATTAAT,,  
5900,AA678160,,20,159,ATTGCAGGATTAAATGGTCT,,  
5901,AA678160,,20,153,GGATTAAATGGTCTCTAATT,,  
30 5902,AA678160,,20,147,AATGGTCTCTAATTATTGT,,  
5903,AA678160,,20,141,CTCTAATTATTGTAGCCAG,,  
5904,AA678160,,20,135,TTTATTGTAGCCAGGTTTT,,  
5905,AA678160,,20,129,GTAGCCAGGTTTTTCATAC,,  
5906,AA678160,,20,123,AGGGTTTTTCATACTAATAC,,  
35 5907,AA678160,,20,117,TTTCATACTAATACTTTTTA,,  
5908,AA678160,,20,111,ACTAATACTTTTTACTTTAT,,  
5909,AA678160,,20,105,ACTTTTTACTTTATTGGAA,,  
5910,AA678160,,20,99,TACTTTATTGGAAAGCGGAC,,  
5911,AA678160,,20,93,ATTGGAAAGCGGACTTGGAT,,  
40 5912,AA678160,,20,87,AAGCGGACTTGGATTGTACT,,  
5913,AA678160,,20,81,ACTTGGATTGTACTAGGGCA,,  
5914,AA678160,,20,75,ATTGTACTAGGGCAATCTT,,  
5915,AA678160,,20,69,CTAGGGCAATCTTTAAAAA,,  
5916,AA678160,,20,63,CAAACTTTAAAAAAGAAA,,  
45 5917,AA678160,,20,57,TTTAAAAAAGAAACATTTA,,  
5918,AA678160,,20,51,AAAAGAAACATTTACAATAA,,  
5919,AA678160,,20,45,AACATTTACAATAATAGAGA,,  
5920,AA678160,,20,39,TACAATAATAGAGAAAAAGA,,  
5921,AA678160,,20,33,AATAGAGAAAAAGACTGTGG,,  
50 5922,AA678160,,20,27,GAAAAAGACTGTGGCCCCAT,,  
5923,AA678160,,20,21,GACTGTGGCCCCATTAAAAA,,  
5924,AA678160,,20,15,GGCCCCATTAAAAAATGCT,,  
5925,AA678160,,20,9,ATTAAAAAATGCTAAATTA,,  
5926,AA678160,,20,3,AAAATGCTAAATTAAGATTG,,  
55 (GENBANK ACCESSION NO. R42770)  
TTTTTTTTTTGTAACCTTAATCTTTTATTTGTTTCATTAATAGAGCAATTTTGATGTGAAGACTAAAAACACACATTTCTGTTTCTTTA  
ATACTCAGTGTATACATTTTGCAGATTAAATTTAAATACGTATTTTGGACAGTTATTTGATANAATTCCTTCAGACGTTGTTTTTCA  
AACCATCATATAAATTTAATATCTGCATTTTCGGTAAGTNCCTCAAACCCCTAGTCAAGGGGAAANCTGTAATCTAATGAATA  
AGGANCTTCTCAGGGCAATTAGGACAATATTNCAAACNNGGCTGCTTGACTCANGGGTGACTTCCTTAAATCCGNGGTTTCTCAGG  
60 CCCCNGACTGTGGGATGTTTTGAGCGGGGTAATNTTTGTTATGGGGGGCTGTCCCTACANCGGGGTTTAGGGGGG  
(SEQ ID NO: 5927)

5928,R42770,,20,411,CCCCCTAAAAACCCGNTGT,,  
5929,R42770,,20,405,TAAAAACCCGNTGTAGGGAC,,  
65 5930,R42770,,20,399,CCCGNTGTAGGGACAGCCCC,,  
5931,R42770,,20,393,GTAGGGACAGCCCCCCCCATA,,  
5932,R42770,,20,387,ACAGCCCCCCCCATAACAAAN,,  
5933,R42770,,20,381,CCCCATAACAAANAATTAC,,  
5934,R42770,,20,375,TAACAAANAATTACCCGCT,,  
70 5935,R42770,,20,369,ANAATTACCCGCTCAAAAC,,  
5936,R42770,,20,363,ACCCGCTCAAAACATCCCA,,  
5937,R42770,,20,357,CTCAAAACATCCACAGTGN,,  
5938,R42770,,20,351,ACATCCCAAGTGNCGGGG,,  
5939,R42770,,20,345,CACAGTGNCGGGGCTGAGA,,  
75 5940,R42770,,20,339,GNCGGGGCTGAGAAACNC,,

5941,R42770,,20,333,GCCTGAGAAAACNCGGATTT,,  
5942,R42770,,20,327,GAAACNCGGATTTAAGGAA,,  
5943,R42770,,20,321,NCGGATTTAAGGAAGTCAAC,,  
5944,R42770,,20,315,TTAAGGAAGTCACCCNTGAG,,  
5 5945,R42770,,20,309,AAGTCACCCNTGAGTCAAGC,,  
5946,R42770,,20,303,CCCTGAGTCAAGCAGCCCN,,  
5947,R42770,,20,297,AGTCAAGCAGCCCNNGTTTGN,,  
5948,R42770,,20,291,GCAGCCCNNGTTTGNAAATAT,,  
5949,R42770,,20,285,CNCTTTGNAAATATTGTCCT,,  
10 5950,R42770,,20,279,GNAAATATTGTCCTAATTGC,,  
5951,R42770,,20,273,ATTGTCCTAATTGCCCTGAG,,  
5952,R42770,,20,267,CTAATTGCCCTGAGAAGNTC,,  
5953,R42770,,20,261,GCCCTGAGAAGNTCCTTATT,,  
5954,R42770,,20,255,AGAAGNTCCTTATTCAATTAG,,  
15 5955,R42770,,20,249,TCCTTATTCAATTAGATTTAC,,  
5956,R42770,,20,243,TCATTAGATTTACAGNTTT,,  
5957,R42770,,20,237,AGATTTACAGNTTTCCCTT,,  
5958,R42770,,20,231,ACAGNTTTCCCTTGACTAG,,  
5959,R42770,,20,225,TTCCCTTGACTAGGGGTTT,,  
20 5960,R42770,,20,219,TTGACTAGGGGTTTGAAGNA,,  
5961,R42770,,20,213,AGGGGTTTGAAGNACTTACC,,  
5962,R42770,,20,207,TTGAAGNACTTACCGAAAAT,,  
5963,R42770,,20,201,NACTTACCGAAAATGCAGAT,,  
5964,R42770,,20,195,CCGAAAATGCAGATATGTTA,,  
25 5965,R42770,,20,189,ATGCAGATATGTTAAATTTA,,  
5966,R42770,,20,183,ATATGTTAAATTTATGATGA,,  
5967,R42770,,20,177,TAAATTTATGATGATGGTTT,,  
5968,R42770,,20,171,TATGATGATGGTTTGAAAAA,,  
5969,R42770,,20,165,GATGGTTTGAAAAACAACGT,,  
30 5970,R42770,,20,159,TTGAAAAACAACGTCTGAAG,,  
5971,R42770,,20,153,AACAACGTCTGAAGGAATTN,,  
5972,R42770,,20,147,GTCTGAAGGAATTNTATCAA,,  
5973,R42770,,20,141,AGGAATTNTATCAAAATACT,,  
5974,R42770,,20,135,TNTATCAAAATACTGGTCCA,,  
35 5975,R42770,,20,129,AAATAACTGGTCCAAAATAC,,  
5976,R42770,,20,123,CTGGTCCAAAATACGTATTT,,  
5977,R42770,,20,117,CAAAATACGTATTTAAATTT,,  
5978,R42770,,20,111,ACGTATTTAAATTTAATCTG,,  
5979,R42770,,20,105,TTAAATTTAATCTGCAAAAT,,  
40 5980,R42770,,20,99,TTAATCTGCAAAATGTATAC,,  
5981,R42770,,20,93,TGCAAAATGTATACACTGAG,,  
5982,R42770,,20,87,ATGTATACACTGAGTATTAA,,  
5983,R42770,,20,81,ACACTGAGTATTAAAGAAAC,,  
5984,R42770,,20,75,AGTATTAAAGAAACAGGAAA,,  
45 5985,R42770,,20,69,AAAGAAACAGGAAATGTGTG,,  
5986,R42770,,20,63,ACAGGAAATGTGTGTTTTTA,,  
5987,R42770,,20,57,AAATGTGTGTTTTTAGTCCTC,,  
5988,R42770,,20,51,TGTTTTTAGTCCTTCACATCA,,  
5989,R42770,,20,45,TAGTCTTCACATCAAAATTG,,  
50 5990,R42770,,20,39,TCACATCAAAATTGCTCTAT,,  
5991,R42770,,20,33,CAAAATTGCTCTATTAATGA,,  
5992,R42770,,20,27,TGCTCTATTAATGAACAAAT,,  
5993,R42770,,20,21,ATTAATGAACAAATAAAAGA,,  
5994,R42770,,20,15,GAACAAATAAAAGATTAAGT,,  
55 5995,R42770,,20,9,ATAAAAGATTAAGTTACAAA,,  
5996,R42770,,20,3,GATTAAGTTACAAAAAAA,,  
(GENBANK ACCESSION NO. H93087)  
AAAACAAAATTCTGCATTTTTATAAACTTGATAAAAAATAGTATTTCAAACGTACAGTCACCAGAAGTACACAGTTATCAAAAAT  
60 GCACACACTTCACCTGGCATCTCCAGCACCTTCAGCTTCTGTGCCTGGTCTGTTTGGCATCTCCATTTCTGCAGGGTTATTCCCT  
CCTTGCCAGCATCAGCTTTCCCTTTTCCCTTTGGGTACCTTCTCCTCTTTGTCAGGGGCTTTTAGGCTTGGGCTCTGGCTTT  
GGAGGAGCAGGTTTCTTTTGGCAGGAAGAGAGGAAAAAGTGAACATCAGTACAATGGACTGAAGAAAACCCACCAACCAA  
CCAAAAGTACCAAGGGTAAGAGAAAGTTTCTCCTCCTCAAAAGTTTGGTGGTTGGCTTCTTCTAGAATGTGGATTTCAGAA  
GCCCACTCAAAATGTCCACTTTGGCTACAGGCATCAGAAAATTCAGAACCCAGCNAACCCCAAGGGGCAAGAGTCCCAAGTAGAGG  
CAATGATTCCAAACAGGCACTAACCATATTCATGGGAAGCCAAAGGGAATGGTTTTTGANGGTTTTAGGTTTCAGGNCAAG  
65 (SEQ ID NO: 5997)  
  
5998,H93087,,20,588,CTTGNCTGAACCTAAAAAC,,  
5999,H93087,,20,582,CTGAACCTAAAAACCTCCA,,  
70 6000,H93087,,20,576,CTAAAAACCTCCAAAAACC,,  
6001,H93087,,20,570,ACCNTCCAAAAACCATTCCT,,  
6002,H93087,,20,564,CAAAAACCATTCCTTGGCT,,  
6003,H93087,,20,558,CCATTCCCTTGGCTTCCCAT,,  
6004,H93087,,20,552,CCTTGGCTTCCCATGAATTA,,  
6005,H93087,,20,546,CTTCCCATGAATTATGGTTA,,  
75 6006,H93087,,20,540,ATGAATTATGGTTAGTGCCT,,

6007,H93087,,20,534,TATGGTTAGTGCCTGGTTTG,,  
6008,H93087,,20,528,TAGTGCCTGGTTTGAATCA,,  
6009,H93087,,20,522,CTGGTTTGAATCATTGCCT,,  
5 6010,H93087,,20,516,TGGAATCATTGCCTCTACTT,,  
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6013,H93087,,20,498,TTGGGACTCTTGCCCCTTGG,,  
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6015,H93087,,20,486,CCCCTTGGGGTTTNGCTGGT,,  
10 6016,H93087,,20,480,GGGGTTTNGCTGGTCTGAA,,  
6017,H93087,,20,474,TNGCTGGTCTGAAATTTCT,,  
6018,H93087,,20,468,GTCTGAAATTTCTGATGCC,,  
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15 6021,H93087,,20,450,CCTGTAGCCAAAGTGGGACA,,  
6022,H93087,,20,444,GCCAAAGTGGGACATTTGAG,,  
6023,H93087,,20,438,GTGGGACATTTGAGTGGGCT,,  
6024,H93087,,20,432,CATTTGAGTGGGCTTCTGGA,,  
6025,H93087,,20,426,AGTGGGCTTCTGGAAATCCA,,  
20 6026,H93087,,20,420,CTTCTGGAAATCCAACATTC,,  
6027,H93087,,20,414,GAAATCCAACATTTCTAGAAG,,  
6028,H93087,,20,408,CAACATTTCTAGAAGAAAGCC,,  
6029,H93087,,20,402,TCTAGAAGAAAGCCAAACCAC,,  
6030,H93087,,20,396,AGAAAGCCAAACCACCAAAA,,  
25 6031,H93087,,20,390,CCAACCACCAAAAACTTTGG,,  
6032,H93087,,20,384,ACCAAAAACTTTGTAGGAGG,,  
6033,H93087,,20,378,AACTTTGTAGGAGGAGGAGA,,  
6034,H93087,,20,372,TGAGGAGGAGGAGAACTTC,,  
6035,H93087,,20,366,GGAGGAGAACTTCTCTTAC,,  
30 6036,H93087,,20,360,GAAACTTCTCTTACCCTTGG,,  
6037,H93087,,20,354,TCCTTACCCTTGGTACTTT,,  
6038,H93087,,20,348,ACCCTTGGTACTTTTGGTTG,,  
6039,H93087,,20,342,GGTACTTTTGGTTGGTTGTG,,  
6040,H93087,,20,336,TTTGGTTGGTTGTGGGTGGT,,  
35 6041,H93087,,20,330,TGGTTGTGGGTGGTTTTCTT,,  
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6044,H93087,,20,312,TTCAGTCCATTGTACTGATG,,  
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40 6046,H93087,,20,300,TACTGATGTTCACTTTTTC,,  
6047,H93087,,20,294,TGTTCACTTTTCTCTCTT,,  
6048,H93087,,20,288,CTTTTCTCTCTTCTGCTG,,  
6049,H93087,,20,282,CCTCTCTTCTGCCCCAAAA,,  
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45 6051,H93087,,20,270,CCAAAAAAGAAACCTGCTC,,  
6052,H93087,,20,264,AAAGAAACCTGCTCCTCCAA,,  
6053,H93087,,20,258,ACCTGCTCCTCCAAAGCCAG,,  
6054,H93087,,20,252,TCCTCCAAAGCCAGGCCCA,,  
6055,H93087,,20,246,AAAGCCAGAGCCCAAGCCTA,,  
50 6056,H93087,,20,240,AGAGCCCAAGCCTAAAAAGG,,  
6057,H93087,,20,234,CAAGCCTAAAAAGGCCCTG,,  
6058,H93087,,20,228,TAAAAAGGCCCTGCAAGA,,  
6059,H93087,,20,222,GGCCCCGCAAGAAAGGGAG,,  
6060,H93087,,20,216,TGCAAGAAAGGGAGAGAAAG,,  
55 6061,H93087,,20,210,GAAGGGAGAGAAAGGTACCCA,,  
6062,H93087,,20,204,AGAGAAAGGTACCCAAAGGGA,,  
6063,H93087,,20,198,GGTACCCAAAGGGAAAAAGG,,  
6064,H93087,,20,192,CAAAGGGAAAAAGGGAAAAAG,,  
6065,H93087,,20,186,GAAAAAGGGAAAAAGCTGATG,,  
60 6066,H93087,,20,180,GGGAAAAAGCTGATGCTGGCA,,  
6067,H93087,,20,174,AGCTGATGCTGGCAAGGAGG,,  
6068,H93087,,20,168,TGCTGGCAAGGAGGGGAATA,,  
6069,H93087,,20,162,CAAGGAGGGGAATAACCTG,,  
6070,H93087,,20,156,GGGGAATAACCTGCAGAAA,,  
65 6071,H93087,,20,150,TAAACCCTGCAGAAAAATGGAG,,  
6072,H93087,,20,144,TGCAGAAAAATGGAGATGCCA,,  
6073,H93087,,20,138,AAATGGAGATGCCAAACAG,,  
6074,H93087,,20,132,AGATGCCAAACAGACCAGG,,  
6075,H93087,,20,126,CAAAACAGACCAGGCACAGA,,  
70 6076,H93087,,20,120,AGACCAGGCACAGAAAGCTG,,  
6077,H93087,,20,114,GGCACAGAAAGCTGAAGGTG,,  
6078,H93087,,20,108,GAAAGCTGAAGGTGCTGGAG,,  
6079,H93087,,20,102,TGAAGGTGCTGGAGATGCCA,,  
6080,H93087,,20,96,TGCTGGAGATGCCAAGTGAA,,  
75 6081,H93087,,20,90,AGATGCCAAGTGAAGTGTGT,,

6082,H93087,,20,84,CAAGTGAAGTGTGTGCATTT,,  
6083,H93087,,20,78,AAAGTGTGTGCATTTTGTATA,,  
6084,H93087,,20,72,GTGCATTTTGTATAACTGTG,,  
6085,H93087,,20,66,TTTGTATAACTGTGTACTTC,,  
5 6086,H93087,,20,60,TAAGTGTGTACTTCTGGTGA,,  
6087,H93087,,20,54,TGTACTTCTGGTGAAGTGTAC,,  
6088,H93087,,20,48,TCTGGTGAAGTGTACAGTTTG,,  
6089,H93087,,20,42,GAAGTGTACAGTTTGAATAC,,  
6090,H93087,,20,36,ACAGTTTGAATACTATTTT,,  
10 6091,H93087,,20,30,TGAATACTATTTTATCA,,  
6092,H93087,,20,24,ACTATTTTATCAAGTTT,,  
6093,H93087,,20,18,TTTATCAAGTTTATATAAA,,  
6094,H93087,,20,12,CAAGTTTATATAAAATGCAG,,  
6095,H93087,,20,6,TTATAAAATGCAGATTTT,,  
15 (GENBANK ACCESSION NO. AA486518)  
GAAGATGAAGGTGTCTCTCAGAGGAAGTTCTGGATGGCAACGAGCTCACCTGGCTGACTGCAACCTGTGCCAAAGTTACACAT  
AGTACAGGTGGTGTGAAGAAGTACCGGGGATTACCATCCCCGAGGCCCTCCGGGGAGTGATCGGTACTTGAGCAATGCCTACG  
CCCGGGAAGAATTCCGCTTCCACCTGTCCAGATGATGAGGAGATCGAGCTCGCTATGAGCAAGTGGCAAGGCCCTCAAATAAGCC  
CCTCCTGGGACTCCCTCAACCCCTCCATTTTCTCCACAAGGCCCTGGTGGTTTCCACATTGCTACCCAATGGACACACTCCAAAA  
20 TGGCCAGTGGGCAGGGAATCCCTGGAGCACTGTTCGGGATGGTGTGGTGGAGAGGGGATGAGGGAAAGAAATGGGGGGCCTGG  
GTCAGATTTTATTGTGGGGTGGGATGAGTAGGACAACATATTTAGTAATAAAATACAGAATAAAATC  
(SEQ ID NO: 6096)

6097,AA486518,,20,481,GATTTTATTCTGTATTTTA,,  
25 6098,AA486518,,20,475,TATTCTGTATTTTATTACTG,,  
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6147,AA486518,,20,181,GGACAGGTGGAAGCAATTC,,  
75 6148,AA486518,,20,175,GTGGAAGCGAATTTCTCCCG,,



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20 6168,AA486518,,20,55,GGCAACAGGTTGCAGTCAGC,,  
6169,AA486518,,20,49,AGGTTGCAGTCAGCCAGGT,,  
6170,AA486518,,20,43,CAGTCAGCCAGGTTGAGCTC,,  
6171,AA486518,,20,37,GCCAGGGTGAGCTCGTTGCC,,  
6172,AA486518,,20,31,GTGAGCTCGTTGCCATCCAG,,  
25 6173,AA486518,,20,25,TCGTTGCCATCCAGAACTT,,  
6174,AA486518,,20,19,CCATCCAGAACTTCTCTG,,  
6175,AA486518,,20,13,AGAACTTCTCTGAGAGAC,,  
6176,AA486518,,20,7,TTCTCTGAGAGACACCTC,,  
6177,AA486518,,20,1,TGAGAGACACCTTCATCTC,,  
30 (GENBANK ACCESSION NO. AA464729)  
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CCCTCCCTCCAACCTGTCTCTAAGTT  
(SEQ ID NO: 6178)  
35 6179,AA464729,,20,180,AACTTAGAGACAGAGTTGGA,,  
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6182,AA464729,,20,162,GAGGGAGGGGACAGGAGAGG,,  
40 6183,AA464729,,20,156,GGGGACAGGAGAGGTTGGGG,,  
6184,AA464729,,20,150,AGGAGAGGTTGGGGTCACGG,,  
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6186,AA464729,,20,138,GGTCACGGTGGAAGGAGGAA,,  
6187,AA464729,,20,132,GGTGAAGGAGGAAGAGAGC,,  
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55 6198,AA464729,,20,66,CCGCCAGCTTCTTATCGCGC,,  
6199,AA464729,,20,60,GCTTCTTATCGCGCTCGCCA,,  
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60 6203,AA464729,,20,36,GCTTCTTGGCCATGGGACCT,,  
6204,AA464729,,20,30,TGGCCATGGGACCTGGATT,,  
6205,AA464729,,20,24,TGGGACCTGGATTGTTTTT,,  
6206,AA464729,,20,18,CTGGATTGTTTTTCTAAAT,,  
6207,AA464729,,20,12,TTGTTTTTCTAAATAAAGTT,,  
65 6208,AA464729,,20,6,TCTAAATAAAGTTGAAAA,,  
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70 CCCCCTGGCCACCTATGCACCAAGTCATCTCTGCAGAAAAGGCATACCACGAGCAGCTGTCCGTGGCAGAGATACCAATGCCTGCT  
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75 6211,AA180912,,20,360,ATCACACTTACCNTCTGGT,,

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6214,AA180912,,20,342,GTGGNAGGCTCAAAAGCAG,,  
5 6215,AA180912,,20,336,AGGCTCAAAAGCAGGCATTG,,  
6216,AA180912,,20,330,AAAAGCAGGCATTGGTGATC,,  
6217,AA180912,,20,324,AGGCATTGGTGATCTCTGCC,,  
6218,AA180912,,20,318,TGGTGATCTCTGCCACCGAC,,  
6219,AA180912,,20,312,TCTCTGCCACCGACAGCTGC,,  
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10 6221,AA180912,,20,300,ACAGCTGCTCGTGGTATGCC,,  
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6225,AA180912,,20,276,CTGCAGAGATGACTGGTGCA,,  
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20 6231,AA180912,,20,240,AGTGGATGCGAGGGTAGGGC,,  
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25 6236,AA180912,,20,210,TCTGGAACCTCTGTCAGGTCC,,  
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6239,AA180912,,20,192,CCACATTGAGGGCCCCGTCA,,  
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30 6241,AA180912,,20,180,CCCCGTCAAAGCGCAGAGAA,,  
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6244,AA180912,,20,162,AAGCTGTGATGGAGGAGACA,,  
6245,AA180912,,20,156,TGATGGAGGAGACAATTTGG,,  
35 6246,AA180912,,20,150,AGGAGACAATTTGGCTAATG,,  
6247,AA180912,,20,144,CAATTTGGCTAATGAGGCGA,,  
6248,AA180912,,20,138,GGCTAATGAGGCGATTGAGG,,  
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40 6251,AA180912,,20,120,GGTTGGTGATGGTTGGGCGC,,  
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6255,AA180912,,20,96,TGTCTAGGTTGCGGCGGCAG,,  
45 6256,AA180912,,20,90,GGTTGCGGCGGCAGATGTCA,,  
6257,AA180912,,20,84,GGCGGCAGATGTCTATAGATT,,  
6258,AA180912,,20,78,AGATGTCTATAGATTGCTTCG,,  
6259,AA180912,,20,72,CATAGATTGCTTCGTTGTCC,,  
6260,AA180912,,20,66,TTGCTTCGTTGTCCACCATG,,  
50 6261,AA180912,,20,60,CGTTGTCCACCATGAAGGCA,,  
6262,AA180912,,20,54,CCACCATGAAGGCACAGTCT,,  
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6265,AA180912,,20,36,CTGAGTGCTCCAGGGTGGTG,,  
55 6266,AA180912,,20,30,GCTCCAGGGTGGTGTGGGTG,,  
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6269,AA180912,,20,12,TGGTCAGGATAGAGTTGTAG,,  
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60 (GENBANK ACCESSION NO. AA436142)  
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65 GAGTGGCATCTCGGATGAGCCGGGGGACAGACCTGGACAGACAGTGTGCTATTGCTGCTGTGGGTAGGAAAATGGGCGTAAAGG  
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70 6273,AA436142,,20,422,TTTCTCCTCCTTTACGCCCCA,,  
6274,AA436142,,20,416,CTCCTTTACGCCCCATTTTCC,,  
6275,AA436142,,20,410,TACGCCCCATTTTCTACCCA,,  
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75 6278,AA436142,,20,392,CACAGCAGCAAAATGACAACG,,

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5 6282,AA436142,,20,368,TGTCCAGGTCTGTCCCCCGG,,  
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10 6288,AA436142,,20,332,ACTCACATTTTTTTCTTCTT,,  
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6296,AA436142,,20,284,TCCAAGAGCCCATCTACAG,,  
6297,AA436142,,20,278,AGCCCATTTCTACAGTGGGTG,,  
20 6298,AA436142,,20,272,TTCTACAGTGGGTGGTTTTG,,  
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6316,AA436142,,20,164,TCAGTTTGTGTCCCTATTG,,  
6317,AA436142,,20,158,TGTGTGTCCTATTGTAGATG,,  
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6325,AA436142,,20,110,ATTCTGAATGCTTTTCCACG,,  
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50 6328,AA436142,,20,92,CGTAGACTTATCTGGAATGT,,  
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6331,AA436142,,20,74,GTGAACACAACCTCTTGGTT,,  
6332,AA436142,,20,68,ACAACCTCTTGGTTAATAGT,,  
55 6333,AA436142,,20,62,CTTTGGTTAATAGTAAATGC,,  
6334,AA436142,,20,56,TAAATAGTAAATGCTTAACT,,  
6335,AA436142,,20,50,GTAAATGCTTAACTGTAGTC,,  
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6337,AA436142,,20,38,CTGTAGTCCTGAGTAGGTGC,,  
60 6338,AA436142,,20,32,TCCTGAGTAGGTGCATTCT,,  
6339,AA436142,,20,26,GTAGGTGCATTCTGTCTGT,,  
6340,AA436142,,20,20,GCATTCTGTCTGTCTCAAT,,  
6341,AA436142,,20,14,CTGTCTGTCTCAATAAATTT,,  
6342,AA436142,,20,8,GTCTCAATAAATTTTACTTT,,  
65 6343,AA436142,,20,2,ATAAATTTTACTTTGTCTGC,,  
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70 CTGCCCGTTCCCGGTCCCGGCAACAACTGGGGTTGTATGCGCTGGAACCCCTGGGATAGTCTTCGGNTTGCCAGCCTGGGCCACAC  
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(SEQ ID NO: 6344)  
  
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75 6346,H05893,,20,408,GAAATGCCTGGTTTACGTTT,,

6347,H05893,,20,402,CCTGGTTTACGTTTGATGAG,,  
6348,H05893,,20,396,TTACGTTTGATGAGGAAACT,,  
6349,H05893,,20,390,TTGATGAGGAAACTGCGGCC,,  
5 6350,H05893,,20,384,AGGAAACTGCGGCCCATTCG,,  
6351,H05893,,20,378,CTGCGGCCCATTCGCCAGTG,,  
6352,H05893,,20,372,CCCATTGCCAGTGCTCTGTC,,  
6353,H05893,,20,366,GCCCAAGTGCTGTCCGTGTG,,  
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6358,H05893,,20,336,GTGGATGTGGTGGGCCCAGG,,  
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6363,H05893,,20,306,GAAGACTATCACAGGGTTCC,,  
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6365,H05893,,20,294,AGGGTTCCAGACGCATACAA,,  
20 6366,H05893,,20,288,CCAGACGCATACAACCCAG,,  
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6370,H05893,,20,264,GTGGGCCACGGGGAAACGGG,,  
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6375,H05893,,20,234,CACTGAGGAGTTTCTTCCTG,,  
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6378,H05893,,20,216,TGTTACCCCATTCCTGGAAG,,  
6379,H05893,,20,210,CCCCATTCCTGGAAGGTTTGT,,  
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35 6381,H05893,,20,198,AGGTTTGTTAATCTTCGGA,,  
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6383,H05893,,20,186,TCTTCGGAAGAACCCCAATT,,  
6384,H05893,,20,180,GAAGAACCCCAATTATGATC,,  
6385,H05893,,20,174,CCCCAATTATGATCTCTAAG,,  
40 6386,H05893,,20,168,TTATGATCTCTAAGTGACCA,,  
6387,H05893,,20,162,TCTCTAAGTGACCAACAGGG,,  
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6390,H05893,,20,144,GGGCTCTGAACTGCAGCTGA,,  
45 6391,H05893,,20,138,TGAACTGCAGCTGATGTTAT,,  
6392,H05893,,20,132,GCAGCTGATGTTATCAGCAG,,  
6393,H05893,,20,126,GATGTTATCAGCAGGACATG,,  
6394,H05893,,20,120,ATCAGCAGGACATGCATCCT,,  
6395,H05893,,20,114,AGGACATGCATCCTGCTGCC,,  
50 6396,H05893,,20,108,TGCATCCTGCTGCCAAGGGT,,  
6397,H05893,,20,102,CTGCTGCCAAGGGTGGACAC,,  
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6399,H05893,,20,90,GTGGACACGGCTGCAGACTT,,  
6400,H05893,,20,84,ACGGCTGCAGACTTCTGGGG,,  
55 6401,H05893,,20,78,GCAGACTTCTGGGGGAATTG,,  
6402,H05893,,20,72,TTCTGGGGGAATTGTCGCCT,,  
6403,H05893,,20,66,GGGAATTGTCGCCTCCTGCT,,  
6404,H05893,,20,60,TGTCGCCTCCTGCTCTTTTG,,  
6405,H05893,,20,54,CTCCTGCTCTTTGTTACTG,,  
60 6406,H05893,,20,48,CTCTTTTGTACTGAGTGAG,,  
6407,H05893,,20,42,TGTTACTGAGTGAGATAAGG,,  
6408,H05893,,20,36,TGAGTGAGATAAGGTTGTTC,,  
6409,H05893,,20,30,AGATAAGGTTGTTCAATAAA,,  
6410,H05893,,20,24,GGTTGTTCAATAAAGACTTT,,  
65 6411,H05893,,20,18,TCAATAAAGACTTTTATCCC,,  
6412,H05893,,20,12,AAGACTTTTATCCCCAAGGT,,  
6413,H05893,,20,6,TTTATCCCCAAGGTNAAAAA,,  
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70 AGAATTTGTGTTTGTCTGCTCTATCTTGTGTTTTTCTTCTGGGGGGGTCTAGAACAGTGCCTGGCACATAGTAGGCGCTCA  
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75 (SEQ ID NO: 6414)

6415,H37989,,20,425,CTTCCTTATATAGTGNCTTC,,  
6416,H37989,,20,419,TATATAGTGNCTTCTACCCA,,  
6417,H37989,,20,413,GTGNCTTCTACCCACTACNC,,  
5 6418,H37989,,20,407,TCTACCCACTACNCTTCTAC,,  
6419,H37989,,20,401,CACTACNCTTCTACCATTTT,,  
6420,H37989,,20,395,NCTTCTACCATTTTCTACTT,,  
6421,H37989,,20,389,ACCATTTTCTACTTTGGGCT,,  
6422,H37989,,20,383,TTCTACTTTGGGCTTAGGAT,,  
10 6423,H37989,,20,377,TTTGGGCTTAGGATGATGGC,,  
6424,H37989,,20,371,CTTAGGATGATGGCCATTAT,,  
6425,H37989,,20,365,ATGATGGCCATTATCTACAT,,  
6426,H37989,,20,359,GCCATTATCTACATGTGTTT,,  
6427,H37989,,20,353,ATCTACATGTGTTTTTCAGCA,,  
15 6428,H37989,,20,347,ATGTGTTTTTCAGCACCTGGT,,  
6429,H37989,,20,341,TTTCAGCACCTGGTTGGTTC,,  
6430,H37989,,20,335,CACCTGGTTGGTTCTAAATG,,  
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6435,H37989,,20,305,ACCCAGCTTCTGGAGATTT,,  
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6437,H37989,,20,293,GGAGATTTTTAAGAGGAAGT,,  
25 6438,H37989,,20,287,TTTTAAGAGGAAGTATTAAC,,  
6439,H37989,,20,281,GAGGAAGTATTAAGTGGACA,,  
6440,H37989,,20,275,GTATTAAGTGGACAAATGGA,,  
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6442,H37989,,20,263,CAAATGGAATGGGCACCAGA,,  
30 6443,H37989,,20,257,GAATGGGCACCAGAAAGAAA,,  
6444,H37989,,20,251,GCACCAGAAAGAAATACAGG,,  
6445,H37989,,20,245,GAAAGAAATACAGGGTCACC,,  
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35 6448,H37989,,20,227,CCCAGAATGGCAGAAACCTA,,  
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6452,H37989,,20,203,TCCCAGAGTGGAAGAGAGAGA,,  
40 6453,H37989,,20,197,AGTGGAAGAGAGAGGAGAC,,  
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50 6463,H37989,,20,137,AGGCACTGTTCTAGACCCCC,,  
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6465,H37989,,20,125,AGACCCCCCCCAGAAAGAAA,,  
6466,H37989,,20,119,CCCCCAGAAAGAAAAACAAA,,  
6467,H37989,,20,113,GAAGAAAAACAAAAACAA,,  
55 6468,H37989,,20,107,AAAAACAAAAACAAGATAGA,,  
6469,H37989,,20,101,AAAAACAAGATAGAGGCAGC,,  
6470,H37989,,20,95,AAGATAGAGGCAGCAACAC,,  
6471,H37989,,20,89,GAGGCAGCAACACAAATTC,,  
6472,H37989,,20,83,GCAAAACACAAATTCGAGGG,,  
60 6473,H37989,,20,77,ACAAATTCTGAGGGAGAGGA,,  
6474,H37989,,20,71,TCTGAGGGAGAGGAAAGGGG,,  
6475,H37989,,20,65,GGAGAGGAAAGGGGTAGTTG,,  
6476,H37989,,20,59,GAAAGGGGTAGTTGAGTAAG,,  
6477,H37989,,20,53,GGTAGTTGAGTAAGACGGCT,,  
65 6478,H37989,,20,47,TGAGTAAGACGGCTAAGGGA,,  
6479,H37989,,20,41,AGACGGCTAAGGGAAGTGA,,  
6480,H37989,,20,35,CTAAGGGAAGTGAAGGCCT,,  
6481,H37989,,20,29,GAAGTGAAGGCCTGAGGTG,,  
6482,H37989,,20,23,AGAAGCCTGAGGTGATGGGG,,  
70 6483,H37989,,20,17,CTGAGGTGATGGGGCTCTNC,,  
6484,H37989,,20,11,TGATGGGGCTCTNCTTAGGC,,  
6485,H37989,,20,5,GGCTCTNCTTAGGCCTCCNC,,  
(GENBANK ACCESSION NO. AA486238)  
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75 GGCTATTAGATCACTAGCACTGCTTTACCGCTCCTCATCGCCAAACACCCCATGCTCTGTGGCCTTCTTACACTCTCAGAGGGCAGA

GTGGCAGCCGGGACCCCTACAGAACTCAGAGGGCAGAGTGGCAGCCAGGCCACATGTCTCTCAAGTACCTGTCCCCTCGCTCTG  
GTGATTATTTCTTGAGAAATCACCACACGAGACCATCCCGGCAGTCATGGTTTTGCTTTAGTTTTCCAAGTCCGTTTCAGTCCCTTCC  
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(SEQ ID NO: 6486)

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6489,AA486238,,20,376,GGCAAGTGGGAAACTGCTCG,,  
6490,AA486238,,20,370,TGGGAACTGCTCGCCACTG,,  
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6492,AA486238,,20,358,CGCCACTGCAGAAATTTCTTC,,  
6493,AA486238,,20,352,TGCAGAAATTTCTTCAGACCA,,  
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6503,AA486238,,20,292,CATGACTGCCGGGATGGTCT,,  
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25 6506,AA486238,,20,274,CTCGTGTGGTGATTCTGCA,,  
6507,AA486238,,20,268,TGGTGATTCTGCAAGAAATA,,  
6508,AA486238,,20,262,TTCTGCAAGAAATAATCACC,,  
6509,AA486238,,20,256,AAGAAATAATCACCAGAGCG,,  
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30 6511,AA486238,,20,244,CCAGAGCGAGGGGACAGGTA,,  
6512,AA486238,,20,238,CGAGGGGACAGGTACTTGAG,,  
6513,AA486238,,20,232,GACAGGTACTTGAGAGACAT,,  
6514,AA486238,,20,226,TACTTGAGAGACATGTGGGC,,  
6515,AA486238,,20,220,AGAGACATGTGGGCCTGGCT,,  
35 6516,AA486238,,20,214,ATGTGGGCCTGGCTGCCACT,,  
6517,AA486238,,20,208,GCCTGGCTGCCACTCTGCCC,,  
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6520,AA486238,,20,190,CCTCTGAGTTTCTGTAGGGT,,  
40 6521,AA486238,,20,184,AGTTTCTGTAGGGTGCCCGG,,  
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6523,AA486238,,20,172,GTGCCCGGCTGCCACTCTGC,,  
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6525,AA486238,,20,160,CACTCTGCCCTCTGAGAAGT,,  
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6527,AA486238,,20,148,TGAGAAGTGAAGAAGGCCA,,  
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50 6531,AA486238,,20,124,GCATGGGGGTGTTGGCGATG,,  
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6535,AA486238,,20,100,CGGTAAAGCAGTGCTAGTG,,  
55 6536,AA486238,,20,94,AAGCAGTGCTAGTGATCTAA,,  
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6538,AA486238,,20,82,TGATCTAATAGCCAAATACA,,  
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6540,AA486238,,20,70,CAAATACATTAACACGGACA,,  
60 6541,AA486238,,20,64,CATTAACACGGACACTGGAA,,  
6542,AA486238,,20,58,CACGGACACTGGAAGAGATT,,  
6543,AA486238,,20,52,CACTGGAAGAGATTAAACGG,,  
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6545,AA486238,,20,40,TTAAGCGGATTTTAAGTCAT,,  
65 6546,AA486238,,20,34,GAATTTTAAGTCATCTCCTT,,  
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6548,AA486238,,20,22,ATCTCCTTTGCCAAATGACA,,  
6549,AA486238,,20,16,TTTGCCAAATGACAACCAAA,,  
6550,AA486238,,20,10,AAATGACAACCAAACTAGGT,,  
70 6551,AA486238,,20,4,CAACCAAACTAGGTGTCCCC,,  
(GENBANK ACCESSION NO. AA504461)  
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AAAAATAATACACAAATGCCAAATGTACACAGTGTACAACCTGAACTGAGAAAGTGCAAGGAGACCAGGGAATGGAAAGTGGGT  
AGGGGTGCGGAGGATGGGCACCAAGGCTGGTGTCTGTACAGCCACACTGGGTGCAAGGCCACGTGTCTCACGGCCAAGGTAACCG



GGTGTCTCAGGCACCTTAATAAATATTAAGGGTGACCGGTGACTCAGGCTCTGCCTCTGGGAAAGTGGCATCATTTGGTGAATGAGTTT  
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(SEQ ID NO: 6552)

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6559,AA504461,,20,304,CCACTTCCCAGAGGCAGAGC,,  
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6562,AA504461,,20,286,GCCTGAGTCACCGGTACCCC,,  
15 6563,AA504461,,20,280,GTACCCGGTCAACCTTAATA,,  
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6571,AA504461,,20,232,CCTTGGCCGTGAGGACACGT,,  
6572,AA504461,,20,226,CCGTGAGGACACGTGGCCTG,,  
25 6573,AA504461,,20,220,GGACACGTGGCCTGCACCCA,,  
6574,AA504461,,20,214,GTGGCCTGCACCCAGGTGTG,,  
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30 6578,AA504461,,20,190,TCAGGACACCAAGCCTGGTGC,,  
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50 6598,AA504461,,20,70,TGCACTGTTTCTGTGCTG,,  
6599,AA504461,,20,64,TGTTTTCTGTGCTGTGTGTT,,  
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6602,AA504461,,20,46,TTGGGATGGGATCACAGGCC,,  
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6604,AA504461,,20,34,CACAGGCCAGGGAAAGCCCG,,  
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6606,AA504461,,20,22,AAAGCCCGTGTCAATGAATG,,  
6607,AA504461,,20,16,CGTGTCAATGAATGCCGGGG,,  
60 6608,AA504461,,20,10,AATGAATGCCGGGACAGAG,,  
6609,AA504461,,20,4,TGCCGGGACAGAGAGGGGC,,  
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65 AGACCAGGGCTGGGTGCAACAGGAGGGTCAACAGAGCCTGGCTGGTGTCCCTGGGCCCCAAAGGGGCTGGGGCTCCATGGGAGA  
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6614,AA448400,,20,419,CTGTTCCTTAGTAAGTCCT,,  
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6616,AA448400,,20,407,TAAGTCCTTCCATGTTCGGCC,,  
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6619,AA448400,,20,389,CCTCTAACCCAGGCCCCGA,,  
5 6620,AA448400,,20,383,ACCCAGGCCCGAGGACCC,,  
6621,AA448400,,20,377,GGCCCCGAGGACCCAGACCC,,  
6622,AA448400,,20,371,GAGGACCCAGACCCAGTGGG,,  
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10 6625,AA448400,,20,353,GGGAGGCGGACGTTCCAGCC,,  
6626,AA448400,,20,347,CGGACGTTCCAGCCGGCATG,,  
6627,AA448400,,20,341,TTCCAGCCGGCATGGCTGGG,,  
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55 6670,AA448400,,20,83,GGAGGTGTGAGGCTGTGGCG,,  
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60 6675,AA448400,,20,53,GGCAGAACCTAACCTGACC,,  
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65 6680,AA448400,,20,23,CTTGGCGGTATCCGCCCCAA,,  
6681,AA448400,,20,17,GTATCCGCCCCCAATAAAAG,,  
6682,AA448400,,20,11,CCCCCAATAAAAGCAATT,,  
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(GENBANK ACCESSION NO. AA480815)  
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25 CCGCTATGTCCAGAAAGGAGAATACAGAACGAATCCTGAAGACATCTACCCAGCAACCCCTACTGGATGATGACGTGAGCAGCGGC  
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65 AATAACTGAGCTTAGAGTATACCTCCTATATGTCCATTTAAGTCAGGAGAGGGGGCGATATAGAGACTAAGGCACAAAATTTGTTT  
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7395,AA463610,,20,11,AAGGAACCAACAACAATTT,,  
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35 ACTTACTACCAGGGCTTTTTCTGT  
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7413,R78585,,20,353,GCCCCACAAGATAAGAACAC,,  
7414,R78585,,20,347,CAAGATAAGAACACTGCAAC,,  
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7523,R33851,,20,20,TTCTGTCAAGACGGTAAGAG,,  
20 7524,R33851,,20,14,CAAGACGGTAAGAGTGCAAG,,  
7525,R33851,,20,8,GGTAAGAGTGCAAGGTGTCA,,  
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25 ATTGCTTTTGCCAAAATACCAGAGCCCTTCAAGTGCCAAACAGAGTATGTCCGATGGTATCTGGGTAAGGAAGGAAAGCAAAAGCAAG  
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7557,R14663,,20,132,ACCCAGATACCATCGGACAT,,  
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7559,R14663,,20,120,TCGGACATACTCTGTTTGGC,,  
7560,R14663,,20,114,ATACTCTGTTTGGCACTTGA,,  
7561,R14663,,20,108,TGTTTGGCACTTGAAGGCTC,,  
7562,R14663,,20,102,GCACTTGAAGGCTCTGGTAT,,  
65 7563,R14663,,20,96,GAAGGCTCTGGTATTTTGGC,,  
7564,R14663,,20,90,CTGGTATTTTGGCAAAAGCA,,  
7565,R14663,,20,84,ATTTTGGCAAAAGCAATTATG,,  
7566,R14663,,20,78,GCAAAAGCAATTATGGGAGGC,,  
7567,R14663,,20,72,CAATTATGGGAGGCCCAATC,,  
70 7568,R14663,,20,66,TGGGAGGCCCAATCTAGAC,,  
7569,R14663,,20,60,GCCCAATCTAGACGGCAAC,,  
7570,R14663,,20,54,TCCTAGACGGCAACTGOGGA,,  
7571,R14663,,20,48,ACGGCAACTGGGGACGAAGG,,  
7572,R14663,,20,42,ACTGGGGACGAAGGAGTCTT,,  
75 7573,R14663,,20,36,GACGAAGGAGTCTTGTGAC,,

7574,R14663,,20,30,GGAGTCTTTGTGACTAGATG,,  
7575,R14663,,20,24,TTTGTGACTAGATGGAAGTC,,  
7576,R14663,,20,18,ACTAGATGGAAGTCTTTCCC,,  
7577,R14663,,20,12,TGGAAGTCTTTCCCCTCTGC,,  
5 7578,R14663,,20,6,TCTTTCCCCTCTGCAGTCTG,,  
(GENBANK ACCESSION NO. R33355)  
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TTGGGGGGGTCTGTATCTTAGGGCCAGCCCTCCTAGTGGGGCCAGCCCCCTAGTGTTAAAAATAGGNCCCTAACCCCCCAGGGGTGA  
CCCCCGTGGGNGGGAATTTACGGGACATCTGAGTGAGTGGGGGGCTAGTGTCAAGTCTTGCCCCCAAGTCAGCCTGGGCCCCCAG  
10 GCTTCTTAGGGAAGGGANGGCCACCCCCCTNCCCTGTGCAAAATGCTTGCAAGTTCCTTAGTCAGTGTCAAGTGTCTT  
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7580,R33355,,20,317,AAACAGCTGACACTGACTAA,,  
7581,R33355,,20,311,CTGACACTGACTAAGGAAGT,,  
15 7582,R33355,,20,305,CTGACTAAGGAAGTGAAGC,,  
7583,R33355,,20,299,AAGGAAGTGAAGCATTTGC,,  
7584,R33355,,20,293,CTGCAAGCATTTGCAACAGG,,  
7585,R33355,,20,287,GCAATTTGCAACAGGNNAGGG,,  
7586,R33355,,20,281,GCAACAGGNNAGGGGGGTGC,,  
20 7587,R33355,,20,275,GGGNAGGGGGGTGCCNTCC,,  
7588,R33355,,20,269,GGGGGTGCCNTCCCTTCCC,,  
7589,R33355,,20,263,GCCNTCCCTTCCCTAAGAA,,  
7590,R33355,,20,257,CCCTTCCCTAAGAAGCCTGG,,  
7591,R33355,,20,251,CCTAAGAAGCCTGGGGGCC,,  
25 7592,R33355,,20,245,AAGCCTGGGGGCCAGGCTG,,  
7593,R33355,,20,239,GGGGGCCAGGCTGACTTGG,,  
7594,R33355,,20,233,CCAGGCTGACTTGGGGGGCA,,  
7595,R33355,,20,227,TGACTTGGGGGGCAAGACT,,  
7596,R33355,,20,221,GGGGGGCAAGACTTGACACT,,  
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7598,R33355,,20,209,TTGACACTAGGCCCCACTC,,  
7599,R33355,,20,203,CTAGGCCCCACTCACTCAG,,  
7600,R33355,,20,197,CCCCACTCACTCAGATGTCC,,  
7601,R33355,,20,191,TCACTCAGATGTCCCTGAAA,,  
35 7602,R33355,,20,185,AGATGTCCCTGAAATTCCCN,,  
7603,R33355,,20,179,CCCTGAAATCCCNCCCACG,,  
7604,R33355,,20,173,AATCCCNCCCACGGGGGTG,,  
7605,R33355,,20,167,CNCCCACGGGGGTCACCCCT,,  
7606,R33355,,20,161,CGGGGGTCACCCCTGGGGGG,,  
40 7607,R33355,,20,155,TCACCCCTGGGGGGTTAGGG,,  
7608,R33355,,20,149,CTGGGGGGTTAGGNCCTAT,,  
7609,R33355,,20,143,GGTTAGGNCCTATTTTAA,,  
7610,R33355,,20,137,GGNCCTATTTTAACTAG,,  
7611,R33355,,20,131,ATTTTAACTAGGGGGCT,,  
45 7612,R33355,,20,125,AACACTAGGGGGCTGGCCCA,,  
7613,R33355,,20,119,AGGGGGCTGGCCCACTAGGA,,  
7614,R33355,,20,113,CTGGCCCACTAGGAGGGCTG,,  
7615,R33355,,20,107,CACTAGGAGGGCTGGCCCTA,,  
7616,R33355,,20,101,GAGGGCTGGCCCTAAGATAC,,  
50 7617,R33355,,20,95,TGGCCCTAAGATACAGACCC,,  
7618,R33355,,20,89,TAAGATACAGACCCCCCAA,,  
7619,R33355,,20,83,ACAGACCCCCCAATCTCCC,,  
7620,R33355,,20,77,CCCCCAATCTCCCCAAAGC,,  
7621,R33355,,20,71,AATCTCCCCAAAGCGGGGAG,,  
55 7622,R33355,,20,65,CCCAAAGCGGGGAGGAGATA,,  
7623,R33355,,20,59,GCGGGGAGGAGATATTTATT,,  
7624,R33355,,20,53,AGGAGATATTTATTTGGGG,,  
7625,R33355,,20,47,TATTTATTTGGGGAGAGTT,,  
7626,R33355,,20,41,TTTTGGGGAGAGTTTGGAGG,,  
60 7627,R33355,,20,35,GGAGAGTTTGGAGGGGAGGG,,  
7628,R33355,,20,29,TTTGGAGGGGAGGAGAAATT,,  
7629,R33355,,20,23,GGGGAGGGAGAAATTTATA,,  
7630,R33355,,20,17,GGAGAATTTATTAATAAAAG,,  
7631,R33355,,20,11,TTTATTAATAAAAGAATCTT,,  
65 7632,R33355,,20,5,AATAAAAGAATCTTANNNT,,  
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CTCAGGTGAGACCAAGATTGTCTATTTGGCTCCACCTTCATCTTGCAQANCACTGATCTCAGATTGCCAAGAACTAGAAGCCACT  
TGCACGGTGTGGCCAGAGCTCAGCTGGATGAGAGGCTGAGATGGGTGGCCAGCTTGATACCAGTCCCTGAAGTGAAGCTGTTTACA  
GGACTGGGGAGGCTCCACCCAGAAGGCTTTCATTTGTACTCTGCTGGGAGTGAAGTGGGAAAACTCCTTCCCTGCTGCTGAGTGGAG  
70 AAGGCTCATCCGGCTTTGACCCACCATCCGTTGCAAGAAGCTCCAGGGAGCAGCAATCCTAAGAGTTGGGAGGCAGCCAAGACC  
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7634,T64626,,20,362,AAAACNACTTCCGGGAAGGT,,  
75 7635,T64626,,20,356,ACTTCCGGGAAGGTTTTGAA,,

7636,T64626,,20,350,GGGAAGGTTTTGAAAAGGAAA,,  
7637,T64626,,20,344,GTGTTGAAAGGAAAGGGGGT,,  
7638,T64626,,20,338,AAAGGAAAGGGGGTCTTGGC,,  
7639,T64626,,20,332,AAGGGGGTCTTGGCTGCCTC,,  
5 7640,T64626,,20,326,GTCTTGGCTGCCTCCCAACT,,  
7641,T64626,,20,320,GCTGCCTCCCAACTCTTAGG,,  
7642,T64626,,20,314,TCCCAACTCTTAGGATTGCT,,  
7643,T64626,,20,308,CTCTTAGGATTGCTGCTCCC,,  
7644,T64626,,20,302,GGATTGCTGCTCCCTGGAGG,,  
10 7645,T64626,,20,296,CTGCTCCCTGGAGGCTTCTG,,  
7646,T64626,,20,290,CCTGGAGGCTTCTGCAACGG,,  
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7649,T64626,,20,272,GGATGGTGGGTCAAAGCCGG,,  
15 7650,T64626,,20,266,TGGGTCAAAGCCGGATGAGG,,  
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7652,T64626,,20,254,GGATGAGGCCTCTCTCCACT,,  
7653,T64626,,20,248,GGCCTCTCTCCACTCAGCAG,,  
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20 7655,T64626,,20,236,CTCAGCAGCAGGGAAGGAGT,,  
7656,T64626,,20,230,AGCAGGGAAGGAGTTTTTCC,,  
7657,T64626,,20,224,GAAGGAGTTTTTCCCAGTCA,,  
7658,T64626,,20,218,GTGTTTTCCCAGTCACTCCCA,,  
7659,T64626,,20,212,CCAGTCACTCCAGCAGAG,,  
25 7660,T64626,,20,206,CACTCCAGCAGAGTACAAA,,  
7661,T64626,,20,200,CAGCAGATACAAATGAAAG,,  
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7663,T64626,,20,188,AATGAAAGCCTTCTGGGTGG,,  
7664,T64626,,20,182,AGCCTTCTGGGTGGAGCCTC,,  
30 7665,T64626,,20,176,CTGGGTGGAGCCTCCCCAGT,,  
7666,T64626,,20,170,GGAGCCTCCCCAGTCTGTA,,  
7667,T64626,,20,164,TCCCCAGTCTGTAAACAGC,,  
7668,T64626,,20,158,GTCTGTAAACAGCTCAGTT,,  
7669,T64626,,20,152,TAAACAGCTCAGTTCAGGGA,,  
35 7670,T64626,,20,146,GCTCAGTTCAGGGAAGTGGTA,,  
7671,T64626,,20,140,TTCAGGGAAGTGGTATACAAG,,  
7672,T64626,,20,134,GACTGGTATACAAGCTGGCC,,  
7673,T64626,,20,128,TATACAAGCTGGCCACCCAT,,  
7674,T64626,,20,122,AGCTGGCCACCCATCTCAGC,,  
40 7675,T64626,,20,116,CCACCCATCTCAGCCTCTCA,,  
7676,T64626,,20,110,ATCTCAGCCTCTCATCCAGC,,  
7677,T64626,,20,104,GCCTCTCATCCAGCTGAGCT,,  
7678,T64626,,20,98,CATCCAGCTGAGCTCTGGCC,,  
7679,T64626,,20,92,GCTGAGCTCTGGCCACACCG,,  
45 7680,T64626,,20,86,CTCTGGCCACACCGTGCAAG,,  
7681,T64626,,20,80,CCACACCGTGCAAGTGCCIT,,  
7682,T64626,,20,74,CGTGCAAGTGCTTCTAGTT,,  
7683,T64626,,20,68,AGTGGCTTCTAGTTTCTTGG,,  
7684,T64626,,20,62,TTCTAGTTTCTTGGCAATCT,,  
50 7685,T64626,,20,56,TTTCTTGGCAATCTGAGATC,,  
7686,T64626,,20,50,GGCAATCTGAGATCAGCTGN,,  
7687,T64626,,20,44,CTGAGATCAGCTGNTCTGCA,,  
7688,T64626,,20,38,TCAGCTGNTCTGCAAGATGA,,  
7689,T64626,,20,32,GNTCTGCAAGATGAAGGTGG,,  
55 7690,T64626,,20,26,CAAGATGAAGGTGGAGCCAA,,  
7691,T64626,,20,20,GAAGGTGGAGCCAAATGACA,,  
7692,T64626,,20,14,GGAGCCAAATGACACAATCT,,  
7693,T64626,,20,8,AAATGACACAATCTGGTCTC,,  
7694,T64626,,20,2,CACAATCTGGTCTCACCTGA,,  
60 (GENBANK ACCESSION NO. AA448261)  
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CTAGGGCAGGGCCAGCCTTCCCTGGGACTGGGTAGTCGGTACCCAGCCTGCCATGCCCCAGCCCCCTTTCCCCACAAAGAGTA  
TCTTGGGGGAGGGGATCGTGGGCAGAACAGGAGGCAATGAGGATGAACATTTGGCGCTGGTAGCAGCAGCAATGACGGATTGTGC  
65 AAGAATGGAACATTGAACA  
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7696,AA448261,,20,344,TGTTCAATGTTCATTCTTC,,  
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70 7698,AA448261,,20,332,CAITCTTCGACAATCCGTCA,,  
7699,AA448261,,20,326,TCGACAATCCGTCAATTGCTG,,  
7700,AA448261,,20,320,ATCCGTCAATTGCTGCTGCTA,,  
7701,AA448261,,20,314,CATTGCTGCTGCTACCAAGCG,,  
7702,AA448261,,20,308,TGCTGCTACCAAGCGCCAAAT,,  
75 7703,AA448261,,20,302,TACCAAGCGCCAAATGTTTCAT,,

7704,AA448261,,20,296,CGCCAAATGTTTCATCCTCAT,,  
7705,AA448261,,20,290,ATGTTTCATCCTCATTGCCTC,,  
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5 7708,AA448261,,20,272,TCCTGTTCTGCCACGATCC,,  
7709,AA448261,,20,266,TCTGCCACGATCCCTCC,,  
7710,AA448261,,20,260,CACGATCCCTCCCCAAGA,,  
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7712,AA448261,,20,248,CCCCAAGATACTCTTTGTGG,,  
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7715,AA448261,,20,230,GGGAAGAGGGGCTGGGGCA,,  
7716,AA448261,,20,224,GAGGGGCTGGGGCATGGCAG,,  
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15 7718,AA448261,,20,212,CATGGCAGGCTGGGTGACCG,,  
7719,AA448261,,20,206,AGGCTGGGTGACCGACTACC,,  
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20 7723,AA448261,,20,182,TCCCAGGGAAGGCTGGCCCT,,  
7724,AA448261,,20,176,GGAAAGGCTGGCCCTGCCCT,,  
7725,AA448261,,20,170,CTGGCCCTGCCCTAGGATG,,  
7726,AA448261,,20,164,CTGCCCTAGGATGCTGCAG,,  
7727,AA448261,,20,158,CTAGGATGCTGCAGCAGAGT,,  
25 7728,AA448261,,20,152,TGCTGCAGCAGAGTGAGCAA,,  
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7731,AA448261,,20,134,AAGGGGGCCGAATCGACCA,,  
7732,AA448261,,20,128,GCCCGAATCGACCATAAAGG,,  
30 7733,AA448261,,20,122,ATCGACCATAAAGGGTGATG,,  
7734,AA448261,,20,116,CATAAAGGGTGAGGGGCCA,,  
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7736,AA448261,,20,104,AGGGGCCACCTCCTCCCCCT,,  
7737,AA448261,,20,98,CACCTCCTCCCCCTGTTCTG,,  
35 7738,AA448261,,20,92,CTCCCCCTGTTCTGTTGGGG,,  
7739,AA448261,,20,86,CTGTTCTGTTGGGGAGGGGT,,  
7740,AA448261,,20,80,TGTTGGGGAGGGGTAGCCAT,,  
7741,AA448261,,20,74,GGAGGGGTAGCCATGATTG,,  
7742,AA448261,,20,68,GTAGCCATGATTTGTCCAG,,  
40 7743,AA448261,,20,62,ATGATTTGTCCCAGCCTGGG,,  
7744,AA448261,,20,56,TGTCCCAGCCTGGGGCTCCC,,  
7745,AA448261,,20,50,AGCCTGGGGCTCCCTCTCTG,,  
7746,AA448261,,20,44,GGGCTCCCTCTCTGGTTTCC,,  
7747,AA448261,,20,38,CCTCTCTGGTTTCTCTATTG,,  
45 7748,AA448261,,20,32,TGGTTTCTATTGTCAGTTA,,  
7749,AA448261,,20,26,CCTATTGTCAGTTACTTGAA,,  
7750,AA448261,,20,20,TGCAGTTACTTGAATAAAAA,,  
7751,AA448261,,20,14,TACTTGAATAAAAAAATAT,,  
7752,AA448261,,20,8,AATAAAAAAATATCCTTTT,,  
50 7753,AA448261,,20,2,AAAAATATCCTTTTCTGGAA,,  
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55 AGAGCCCGGA  
(SEQ ID NO: 7754)

7755,R44202,,20,252,TCCGGGCTCTCTCACCCAGC,,  
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60 7757,R44202,,20,240,CACCCAGCCCTGGTACTGAA,,  
7758,R44202,,20,234,GCCCTGGTACTGAAGGTGCC,,  
7759,R44202,,20,228,GTACTGAAGGTGCCAGACG,,  
7760,R44202,,20,222,AAGGTGCCAGACGTGCTCC,,  
7761,R44202,,20,216,CCCAGACGTGCTCCCTGCTG,,  
65 7762,R44202,,20,210,CGTGCTCCCTGCTGACCTTC,,  
7763,R44202,,20,204,CCCTGCTGACCTTCTGCGGC,,  
7764,R44202,,20,198,TGACCTTCTGCGGCTCCGGG,,  
7765,R44202,,20,192,TCTGCGGCTCCGGGCTGTGT,,  
7766,R44202,,20,186,GCTCCGGGCTGTGTCCCTAA,,  
70 7767,R44202,,20,180,GGCTGTGTCCCTAAATGCAA,,  
7768,R44202,,20,174,GTCCCTAAATGCAAAGCACA,,  
7769,R44202,,20,168,AAATGCAAAGCACANCTCG,,  
7770,R44202,,20,162,AAAGCACANCTCGCCGAGC,,  
7771,R44202,,20,156,CANCTCGCCGAGCCTGCGC,,  
75 7772,R44202,,20,150,CGCCGAGCCTGCGCCCTGAC,,



7773,R44202,,20,144,GCCTGCGCCCTGACATGCTA,,  
7774,R44202,,20,138,GCCCTGACATGCTAACCTCT,,  
7775,R44202,,20,132,ACATGCTAACCTCTCTGAAC,,  
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5 7777,R44202,,20,120,CTCTGAACTGCAACACTGGA,,  
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7780,R44202,,20,102,GATTGTCTTTTTTAAGACT,,  
7781,R44202,,20,96,TCTTTTTTAAGACTCAATCA,,  
10 7782,R44202,,20,90,TTAAGACTCAATCATGACTT,,  
7783,R44202,,20,84,CTCAATCATGACTTCTTTAC,,  
7784,R44202,,20,78,CATGACTCTTTACTAACAC,,  
7785,R44202,,20,72,TTCTTTACTAACACTGGCTA,,  
7786,R44202,,20,66,ACTAACACTGGCTAGCTATA,,  
15 7787,R44202,,20,60,ACTGGCTAGCTATATTATCT,,  
7788,R44202,,20,54,TAGCTATATTATCTTATATA,,  
7789,R44202,,20,48,TATTATCTTATATACTAATA,,  
7790,R44202,,20,42,CTTATATACTAATATCATGT,,  
7791,R44202,,20,36,TACTAATATCATGTTTTAAA,,  
20 7792,R44202,,20,30,TATCATGTTTTAAAAATATA,,  
7793,R44202,,20,24,GTITTTAAAAATATAAAATAG,,  
7794,R44202,,20,18,AAAATATAAAATAGAAATTA,,  
7795,R44202,,20,12,TAAAATAGAAATTAAGAATC,,  
7796,R44202,,20,6,AGAAATTAAGAATCTAAAAA,,  
25 (GENBANK ACCESSION NO. W81570)  
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ACCTGCANCCGCGGCCCTGGTGGCATTGNTGGATGGCCGGGACTGCACAGTGAGATGCCCATCCTGAAGGACGTGGCCACTGTG  
GCTTCTGCGACCGCGCAGTCCACGCGAGGATCCCATGAGAAGGCTCTGAACGAGGCTGTGGGGGCCCTGATGTACCAACACCATCACT  
CTCACCAGGGAGGACCTGGAGAAGTTCAAAGCCCTCCGCATCATCGTCCGGATTGGCAGTGGTTTTGACAACATCGACATCAAGTC  
30 GGCCGGGGATTITAGGCATTTCGCCGTTCTGCAACGTGCCCGCGCGCTTCTGTTGGGAGGAGACGGCCGACTTCGA  
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7799,W81570,,20,394,TCGGCCGTCTCCTCCCAACA,,  
35 7800,W81570,,20,388,GTCTCCTCCCAACAGAACGC,,  
7801,W81570,,20,382,TCCCAACAGAACGCCGCGGG,,  
7802,W81570,,20,376,CAGAACGCCGCGGGCACGTT,,  
7803,W81570,,20,370,GCCGCGGGCACGTTGCAGAA,,  
7804,W81570,,20,364,GGCACGTTGCAGAACGGCAA,,  
40 7805,W81570,,20,358,TTGCAGAACGGCAAAATGCCT,,  
7806,W81570,,20,352,AACGGCAAAATGCCTAAAATC,,  
7807,W81570,,20,346,AAATGCCTAAAATCCCCGGC,,  
7808,W81570,,20,340,CTAAAAATCCCCGGCCGACTT,,  
7809,W81570,,20,334,TCCCCGGCCGACTTGATGTC,,  
45 7810,W81570,,20,328,GCCGACTTGATGTCGATGTT,,  
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7814,W81570,,20,304,AAACCACTGCCAATCCGGAC,,  
50 7815,W81570,,20,298,CTGCCAATCCGGACGATGAT,,  
7816,W81570,,20,292,ATCCGGACGATGATGCGGAG,,  
7817,W81570,,20,286,ACGATGATGCGGAGGGCTTT,,  
7818,W81570,,20,280,ATGCGGAGGGCTTTGAACCT,,  
7819,W81570,,20,274,AGGGCTTTGAACCTCTCCAG,,  
55 7820,W81570,,20,268,TTGAACCTCTCCAGGTCCTC,,  
7821,W81570,,20,262,TTCTCCAGGTCCTCCCTGGT,,  
7822,W81570,,20,256,AGGTCCTCCCTGGTGAGAGT,,  
7823,W81570,,20,250,TCCCTGGTGAGAGTGATGGT,,  
7824,W81570,,20,244,GTGAGAGTGATGGTGTGGTA,,  
60 7825,W81570,,20,238,GTGATGGTGTGGTACATCAG,,  
7826,W81570,,20,232,GTGTGGTACATCAGGGCCCC,,  
7827,W81570,,20,226,TACATCAGGGCCCCACAGC,,  
7828,W81570,,20,220,AGGGCCCCACAGCCTCGTT,,  
7829,W81570,,20,214,CCACAGCCTCGTTCAGGAC,,  
65 7830,W81570,,20,208,GCCTCGTTCAGGACCTTCTC,,  
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7832,W81570,,20,196,ACCTTCTCATGGATCTCCTG,,  
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70 7835,W81570,,20,178,TGCGTGGAAGTGCAGAGCC,,  
7836,W81570,,20,172,GACTGCGGTGCGAGAGCC,,  
7837,W81570,,20,166,GCGTGCAGAGGCCACAGTG,,  
7838,W81570,,20,160,CAGAGGCCACAGTGGCCACG,,  
7839,W81570,,20,154,CCACAGTGGCCACGTCCTTC,,  
75 7840,W81570,,20,148,TGGCCACGTCCTTCAGGATG,,

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7842,W81570,,20,136,TCAGGATGGGCATCTCCACT,,  
7843,W81570,,20,130,TGGGCATCTCCACTGTGCAG,,  
7844,W81570,,20,124,TCTCCACTGTGCAGTCCCGG,,  
5 7845,W81570,,20,118,CTGTGCAGTCCCGGCCATCC,,  
7846,W81570,,20,112,AGTCCCGGCCATCCANCAAT,,  
7847,W81570,,20,106,GGCCATCCANCAATGCCACC,,  
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10 7850,W81570,,20,88,CCAGGGGCCGCGNTGCAGG,,  
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7857,W81570,,20,46,NGACCCAAAGCGGCAGGCCCT,,  
7858,W81570,,20,40,AAGCGGCAGGCCCTTGTGTA,,  
7859,W81570,,20,34,CAGGCCCTTGTGAGCAAGT,,  
20 7860,W81570,,20,28,CTTGTGAGCAAGTGCAGT,,  
7861,W81570,,20,22,GAGCAAGTGCAGTGTGTCN,,  
7862,W81570,,20,16,GTGCGAGTGTGTCNCGAGA,,  
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25 (GENBANK ACCESSION NO. AA128561)  
ATTAGAAAAAACTTCTTTAATGGGAAATTTTACGATTGAAATGATGTTTCATCTTATAGACCACAAACAAATGTTTTAGACAT  
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CTGTGTCCCCAGCATCAGGTTTTCTGTTTTCCCTCTTCTCCCTTTATTCCTTCCCTGTCCTTGTCCATTGCCCTCAACCTCTTTTCTGTTTGTCT  
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30 GGAATGTGGAINTACATATAACCATAGAAACCTATCATCACTCTAGAGGGGAAGTGAATTTCTTAAT  
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7866,AA128561,,20,402,ATTAAGAAATTCACCTCCCC,,  
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35 7868,AA128561,,20,390,ACTTCCCTCTAGGAGGTGA,,  
7869,AA128561,,20,384,CCTCTAGGAGGTGATGATAG,,  
7870,AA128561,,20,378,GGAGGTGATGATAGGGTTTC,,  
7871,AA128561,,20,372,GATGATAGGGTTTCTAATGG,,  
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40 7873,AA128561,,20,360,TCTAATGGTTATATGTANAT,,  
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7875,AA128561,,20,348,ATGTANATCCACATTCCCCA,,  
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7877,AA128561,,20,336,ATTCCCCATTGCTTAGAAA,,  
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7880,AA128561,,20,318,AAGTCTGATTGTAGCTATGA,,  
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60 7893,AA128561,,20,240,AACAGAAAAAGAGGTTGAG,,  
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70 7903,AA128561,,20,180,CAGAAAAACCTGATGCTGGGG,,  
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75 7908,AA128561,,20,150,AGCTCAAGACGTCAACCTCC,,

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5 7913,AA128561,,20,120,CAGAAAATGGCACTTGGGGG,,  
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7925,AA128561,,20,48,GTGGTCTATAAGATGAAACA,,  
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7927,AA128561,,20,36,ATGAAACATCATTTCAATCG,,  
20 7928,AA128561,,20,30,CATCATTTCAATCGTAAAAAT,,  
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30 CCAGCCTGGCCAAACATGGCGGAAACCCCGTCTCTACTAAACATACAAAAATCAGTTGGGCATGGTGGCGTGTGCTGTAGTCCCAGC  
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35 7934,N58473,,20,572,TCGGCACGNGACCAACATGC,,  
7935,N58473,,20,566,CGNGACCAACATGCCTAGTA,,  
7936,N58473,,20,560,CAACATGCCTAGTATTTTAG,,  
7937,N58473,,20,554,GCCTAGTATTTAGTTAGAG,,  
7938,N58473,,20,548,TATTTTAGTTAGAGATGAAT,,  
40 7939,N58473,,20,542,AGTTAGAGATGAATTGCTTT,,  
7940,N58473,,20,536,AGATGAATTGCTTTGATGNG,,  
7941,N58473,,20,530,ATTGCTTTGATGNGATTTTT,,  
7942,N58473,,20,524,TTGATGNGATTTTTTTCTT,,  
7943,N58473,,20,518,NGATTTTTTTCTTTTCTG,,  
45 7944,N58473,,20,512,TTTTTCTTTTCTGCAATGA,,  
7945,N58473,,20,506,TTTTTCTGCAATGAAGCTAT,,  
7946,N58473,,20,500,TGCAATGAAGCTATGTCCAA,,  
7947,N58473,,20,494,GAAGCTATGTCCAAAGAATG,,  
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50 7949,N58473,,20,482,AAAGAAATGTACTTTTCTTTT,,  
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7968,N58473,,20,368,TTAGTAGAGACGGGGTTTCG,,  
70 7969,N58473,,20,362,GAGACGGGGTTTCGCCATGT,,  
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5 7979,N58473,,20,302,CCTGCCTCAGCCTCCCAACA,,  
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20 7994,N58473,,20,212,TTTTCTGTGCTTAGAAAT,,  
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25 7999,N58473,,20,182,TATTCAGAGAACCAGAGAAA,,  
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8001,N58473,,20,170,CAGAGAACTAAAGTGTGTA,,  
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30 8004,N58473,,20,152,TACATTTCCAGTCAAAAAA,,  
8005,N58473,,20,146,TCCAGTCAAAAAAATAC,,  
8006,N58473,,20,140,TCAAAAAAATACGATAAA,,  
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35 8009,N58473,,20,122,AAAAATATTGACTATGAGCAG,,  
8010,N58473,,20,116,TTGACTATGAGCAGATATAT,,  
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40 8014,N58473,,20,92,TGGATTGTCTGTTAATTATC,,  
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8016,N58473,,20,80,TAATTATCCGTGTTACATG,,  
8017,N58473,,20,74,TCCGTGTTACATGCAGTGA,,  
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45 8019,N58473,,20,62,TGCAGTGAGTAATATTGGC,,  
8020,N58473,,20,56,GAGTAATATTGGCACATT,,  
8021,N58473,,20,50,TATTTGGCACATTTTTTCT,,  
8022,N58473,,20,44,GCACATTTTTTCTACATTC,,  
8023,N58473,,20,38,TTTTTCTACATTCCTTATT,,  
50 8024,N58473,,20,32,CTACATTCCTTATTTTCATC,,  
8025,N58473,,20,26,TCCTTATTTTCATCCAGAGT,,  
8026,N58473,,20,20,TTTCATCCAGAGTATAATT,,  
8027,N58473,,20,14,TCCAGAGTATAATTAATGTC,,  
8028,N58473,,20,8,GTATAATTAATGTCTTAATA,,  
55 8029,N58473,,20,2,TTAATGTCTTAATATACCCA,,  
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60 ATTCCAGCCTTTGTGTGGAAGGAGTTGCAATTCITAGGAAACATCTAACTGTTACCTAAACCATAAAATTTCTATCTACTCCA  
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65 8031,AA679352,,20,458,TGGCGAAGCATTCAGTGCCA,,  
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8034,AA679352,,20,440,CACGTTTTAGGTTAAATCCC,,  
8035,AA679352,,20,434,TTAGGTTAAATCCCTGCCAT,,  
70 8036,AA679352,,20,428,TAAATCCCTGCCATATGGGA,,  
8037,AA679352,,20,422,CCTGCCATATGGGACTGTCA,,  
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8039,AA679352,,20,410,GACTGTGAGGAGATCCTACT,,  
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75 8041,AA679352,,20,398,ATCCTACTTAGTATGATCTT,,

8042,AA679352,,20,392,CTTAGTATGATCTTGGCTAG,,  
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20 8061,AA679352,,20,278,TCTCATCATTTTGTTTTCTT,,  
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65 8106,AA679352,,20,8,TTGTCAAGTAAAAAAAAAA,,  
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70 CCAGGTTTGTACATGTCTCTCTGTTTACATCTGGGAGAAAGGTTGCTGCGCATCAGTCGACGAGCTGCACTTCTCTTGACGCCCT  
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8110,N55459,,20,225,CNTGCAAGAAAGAGCTGCTGC,,  
75 8111,N55459,,20,219,AGAAGAGCTGCTGCTCCTGC,,

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8114,N55459,,20,201,GCNTGCCCGTGGGCTGTAGC,,  
8115,N55459,,20,195,CCGTGGGCTGTAGCAAGTGT,,  
5 8116,N55459,,20,189,GCTGTAGCAAGTGTGCCAG,,  
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8118,N55459,,20,177,GTGCCAGGGCTGTGTNGC,,  
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20 8131,N55459,,20,99,AGATGTAAACAGAGACAT,,  
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8137,N55459,,20,63,TTTTTTTATACCACCTTGAC,,  
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30 8141,N55459,,20,39,TTGCTACATTCCTTTTCCTG,,  
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8143,N55459,,20,27,TTTCTGTGAAATATGTGA,,  
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8145,N55459,,20,15,ATATGTGAGTGATAATTAAA,,  
35 8146,N55459,,20,9,GAGTGATAATTAAACACTT,,  
8147,N55459,,20,3,TAATTAACACTTTAGACCT,,  
(GENBANK ACCESSION NO. AA150500)  
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40 GGAGATTTGATAGAGCTCCATCGTTGCCCTCCCATCTTCCACCGAGCTGTGTCCAAGCAGGCTGTCTGGATGCTCTTGTGCAGGAG  
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25 8272,H16833,,20,71,TGTGTATGAGACTAGNCTTT,,  
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8275,H16833,,20,53,TTACAACCTGCTTTGATGGC,,  
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8280,H16833,,20,23,CAATAAATGTCACAATCCCT,,  
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35 8282,H16833,,20,11,CAATCCCTTCTATAGCCCC,,  
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8439,AA001432,,20,11,TAAAAATGCAGTGAGTCC,,  
8440,AA001432,,20,5,ATGCAGTGAGTCCCTTAAAA,,  
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70 8445,H87536,,20,300,GATTGCCCCGATGNCATN,,  
8446,H87536,,20,294,CCGTAGNCCCCATNCTAGAG,,  
8447,H87536,,20,288,NCCCCATNCTAGAGTTCATG,,  
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75 8450,H87536,,20,270,TGGATNTGTTACTGACCC,,

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 5 8455,H87536,,20,240,CAAACAGAAAAAGAGGTTG,,  
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 10 8460,H87536,,20,210,ACAAGGAAGGAATAAAGGGA,,  
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 8468,H87536,,20,162,TGGGGACACAGCATCAGCTC,,  
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 30 8480,H87536,,20,90,GCAAGTTGGTCTTTANCCNCT,,  
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 40 8490,H87536,,20,30,AAACATCATTTCAANCGTAA,,  
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 8492,H87536,,20,18,AANCGTAAATTTCCCATTA,,  
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 50 CCATCTGTAGGGCGTACGGGCGCTCCACCTCCCTCAGGCTGTTCTCCAAGCTGGCCTTCAGATTTCTCATGGAGTCCAGGTCGATCTCC  
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 70 8510,AA664179,,20,551,GGAAGACCCGAGAGGAGCTA,,  
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 75 8515,AA664179,,20,521,GGTCTCAGCAGATGAGGAGA,,

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5 8520,AA664179,,20,491,GTCAACACACAGTCTGTGTA,,  
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25 8540,AA664179,,20,371,CAGCCTGAGGGAGGTGGAGG,,  
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45 8560,AA664179,,20,251,TATGAGGCCCTGCTGAACAT,,  
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55 8570,AA664179,,20,191,CTGCTGGAAGATGGCGAGGA,,  
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60 8575,AA664179,,20,161,GGTGATGCCTTGGACAGCAG,,  
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75 8590,AA664179,,20,71,AATGACACCAAAGTTCTGAG,,



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5 8595,AA664179,,20,41,AGCAGAAGCAGGGTACCCTT,,  
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15 ACTACACCCAAAGTGTCTACAAACCACATGCAGAAAGCACAAGCCCTACCCGTCCATCGAGGAGTTCTCTGGGTGCGNGATGGCAGGCT  
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8638,H86812,,20,90,TAGACTCGCTCAGGCACCTT,,  
55 8639,H86812,,20,84,CGCTCAGGCACCTTTGGGCGA,,  
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65 8649,H86812,,20,24,GGCCAGGAAGAGGCATCTG,,  
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25 8674,AA626698,,20,551,ACCAATGCCTGCTTCGAGCC,,  
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14161 GTCTGTCCACTGGCGGTACA  
14162 TGGCGGTACAGCTCCAGCGG  
14163 GCTCCAGCGGCTTGGTGGGG  
14164 CTTGGTGGGGTTGCTGAGGT  
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14168 CGGAGGACCTGGATGCGGTC  
14169 GGATGCGGTGCGAGTAGTTA  
75 14170 GGAGTAGTTATCTAGCAGGA

14171 TCTAGCAGGAGGACCCCTGA  
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14173 GCTGGTCACTTTCTTGGTCT  
5 14174 TTCTTGGTCTCCACCATGGT  
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14176 CTTCAAGGTCAAGCAGGAGGG  
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14178 TCATGTGCTTGGACATGTCC  
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10 14180 GTGGCCAGCACCATGTGAT  
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14182 GACCATCTTGCCTAGGCTCT  
14183 CGTAGGCTCTGCCGCTGGCG  
14184 GCCGCTGGCGCTTGTGAGG  
15 14185 CTTGCTGAGGTTCTGGAAGA  
14186 TTCTGGAAGATGTGCAAGT  
14187 TGTGCAAGTTGTCTCCTGC  
14188 GTCCTCCTGCAGCAGCTTGA  
14189 AGCAGCTTGAAGCCACGGC  
20 14190 AGCCCAAGGCCAGGTGGTGA  
14191 CAGGTGGTGATTTCTGAGCA  
14192 TTCTGAGCAGCGACTCATC  
14193 CCGACTCATCGTTGTACATG  
14194 GTTGTACATGAGCGCCAGCT  
25 14195 AGCGCCAGCTCCGAATTGGT  
14196 CCGAATTGGTGTGATGAGG  
14197 GTTGATGAGGAAGTGGTGG  
14198 AACTGGTTGGAGACCCAGG  
14199 AGACCCAGGGTGATCCACA  
30 14200 GTGATCCACATCGTGGATGG  
14201 TCGTGGATGGCAGCCGCGAA  
14202 CAGCCGCGAAGAGGGCGGCG  
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14204 AGAATCTCCAGGTCCGTGAA  
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14206 CACTGCATCTAGTGCAGGCG  
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14208 TGGCCAGCAGTACGTGGGTG  
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40 14210 GACTGCAGCAGCTCAGCTGC  
14211 CGTCAGCTGCGTGCAGGCTG  
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14213 TTATGGTAGGCCACGTGAGC  
14214 CCACGTGAGCGTGGTAGTGA  
45 14215 GTGGTAGTGATCCTCCAGCG  
14216 TCCTCCAGCGTCAGCATGTA  
14217 TCAGCATGTATGTCAACATC  
14218 TGTACCATCGTGTCCACCG  
14219 GTGTCCACCGGATGCGGAA  
50 14220 GGATGCGGAATTTCTTCAGC  
14221 TTCTTCAGCAGGTCCCGCT  
14222 AGGTCCCGCTCCTGGAATAT  
14223 CCTGGAATATCATGTACATG  
14224 CATGTACATGATGCAGGTGA  
55 14225 ATGCAGGTGAGTGAGCGGCC  
14226 GTGAGCGGCCCTCCAGCGTAA  
14227 TCCAGCGTAATCCGACACGC  
14228 TCCGACACGCAAAAGATGTT  
14229 AAAAGATGTTCAAGCCCCAC  
60 14230 CAGGCCCACTTGTTCAGGT  
14231 TTGTTCAAGTTCTCCAGTTC  
14232 TCTCCAGTTCTTGGGCCAGG  
14233 TTGGGCCAGGAGCTTCTTT  
14234 AGCTCTTCTTGATCGGTCTT  
65 14235 GATCGGTCTTACCCCAAAT  
14236 CACCCCAAATCGGGGAATGT  
14237 CGGGGAATGTTAGAGTTGTT  
14238 TAGAGTTGTTCAAGGCTGTTA  
14239 CAGGCTGTTACTATGCATCA  
70 14240 CTATGCATCAACTTTTTCAA  
14241 ACTTTTTCAACCCTGTGATT  
14242 CCCTGTGATTTGGGACATGG  
14243 TGGGACATGGGCTGTAAGTG  
14244 GCTGTAAGTGTGGTACAGGG  
75 14245 TGGTACAGGGGGCGGGGGCG



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 14252 GTGGGTGATGGGATCTCCAC  
 14253 GGATCTCCACTTCATTCTGT  
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 10 14255 TTGTCCAGGAATGTTGTGGA  
 14256 ATGTTGTGGAATGTACTCT  
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 14258 GAGACCTGGTTCCGGACCT  
 14259 TTCCGGACCTGCTCATTCT  
 15 14260 GCTCATTCTGACAGGTGTG  
 14261 GACAGGTGTGTGAGCTCACG  
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 14263 GTTCAACATCCTTTGAACT  
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 14301 ACCTCCACCTCCTGAATTCA  
 14302 CCTGAATTCAAGTGATTCTC  
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 14304 CTGCCTCAGCCTCCCCAGTA  
 14305 CTCCCCAGTAGCTGGGATTA  
 14306 GCTGGGATTACAGGCACCCG  
 14307 CAGGCACCCGCCACCATGCC  
 65 14308 CCACCATGCCAGCCAATTT  
 14309 CAGCCAATTTTGTATTTTT  
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 14316 CCTCAGGTGATCCACCTGCC  
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14322 GTGCTCGGCCTCAGAGCCCC  
5 14323 TCAGAGCCCCGTCTCTTCC  
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14325 TTTCTTCTCTTTTCTTTT  
14326 TTTTCTTTTATTTTAGAC  
14327 ATTTTATAGACAGGATCTTGC  
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14330 AGGCTGGAGTGCAGTGATGC  
14331 GCAGTGATGCAGTCATAGCT  
14332 AGTCATAGCTCTTTCAGCC  
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14334 TCCAACCTCTGGGCTCAAGC  
14335 GGGCTCAAGCGATCCCCTT  
14336 GATCCCCTTTGTCTCAACCT  
14337 GTCTCAACCTTCTGAGTAGC  
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14339 TGGGATTCTCAGGTGCACAC  
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14342 GGCTAAATTTTTCAGAT  
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14350 CTCCACCTCAGCCTCCCAA  
14351 AGCCTCCCAAAGTACCGGGA  
14352 AGTACCGGGATTACAGGCAT  
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14354 AAGCCACTATGCCTTGCCCA  
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14356 GCCCTTCTTTCTGCTCCTC  
14357 TCTGCTCCTCTTCTGCCCC  
40 14358 TTCTGCCCCCTACCGTAGT  
14359 CTACCGTAGTTTCAGAAACA  
14360 TTCAGAAACAAAACCTGGGTA  
14361 AAACTGGGTATGAGTGAAGC  
14362 TGAGTGAAGCTTTGGTGCTG  
45 14363 TTTGGTGCTGAAAATTTTCC  
14364 AAAATTTTCCCACTCACAT  
14365 CCACTCACATTTCCATGCTC  
14366 TTCCATGCTCTTGACAGAGAG  
14367 TTGCAGAGAGCCGCTTGGA  
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14370 GGGAGATGCCCTTTGGGATGG  
14371 TTTGGGATGGTCTCCTGACT  
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14374 TGTGCAGGGCTACTACAGAG  
14375 TACTACAGAGGCAGAAAGCT  
14376 GCAGAAAGCTGGCCCGAAGT  
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14379 TAAATATTTGATAAAGAAGG  
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14381 AAATAATTAAGTGACAGATG  
14382 GTGACAGATGTGACTCAAGA  
65 14383 TGACTCAAGAGTGACCACTG  
14384 GTGACCACTGGAGAGGGTGG  
14385 GAGAGGGTGGACTAGAGGCT  
14386 ACTAGAGGCTCCAGCAGACA  
14387 CCAGCAGACAGCACCTCTCC  
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14389 TCACAGGGATAGAAGCCCAG  
14390 AGAAGCCCAGGAGAAAGACA  
14391 GAGAAAGACACCAGGGCATC  
14392 CCAGGGCATCGTAAGAGGCT  
75 14393 GTAAGAGGCTGCCCCTAGA

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14395 GAGCTCTTTTAGGCAAGTCT  
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14397 AGGGTCAGAGTGGACCCAG  
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14400 CCAATTAGACCCTGGGAGCC  
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14406 GAAAGTGAAGCAGGAGCCAC  
14407 CAGGAGCCACATGGAGCCTC  
15 14408 ATGGAGCCTCTTCTGGAAA  
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14412 AGGGCTTTACCATCCATTGC  
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14419 AAGTCCCAGGGTCTGGGCC  
14420 GGTCTGGGCCGGCTTCAGGG  
14421 GGCTTCAGGGGACAGGAGTT  
14422 GACAGGAGTTCAGTGTCAAG  
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14430 CTCTTCTCTGCCTCTCTCCA  
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14444 CCTGTGCATCTGGGTGGACC  
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14447 AAGTCTCCACAGTGGGTGA  
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14451 CACCTGGGACTTCTCCACTG  
14452 TTCTCCACTGAGGCCGTATG  
60 14453 AGGCCGTATGCTTGTACACAC  
14454 CTTGTACACATGGGACTGA  
14455 ATGGGACTGATGTCCAGGCC  
14456 TGTCCAGGCCGACTCACGC  
14457 CGACTCACGCTCGCGGTCTC  
65 14458 TCGCGGTCTCCCTGCTGGAA  
14459 CCTGCTGGAAAGAACTCGGCC  
14460 GAACTCGGCCATGATGCGGT  
14461 ATGATGCGGTCCGTCCACTG  
14462 CCGTCCACTGGCGGTACAGG  
70 14463 GCGGTACAGGGGCAGCGGCT  
14464 GGCAGCGGCTTGGTGGGGTT  
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14466 GCTCAGATCAGCAGTGCA  
14467 GCACAGTGCAACAGGTTCTG  
75 14468 CCAGGTTCTGCAAGACCTGG

14469 CAAGACCTGGATTCCGGTCGG  
14470 ATTCGGTCGGAATAGTTGTC  
14471 AATAGTTGTCCAGGAGGAGG  
5 14472 CAGGAGGAGGACACCGAGGC  
14473 ACACCGAGGCTTGTACCTT  
14474 TTGTACCTTCTTGGTCTCC  
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14476 ACCATGGTCTTGAGGTCGGC  
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14479 ATGTGTTTGGACATGTCTGT  
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14482 ATGTCAATGACCATCCTGCG  
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14486 CGCTGAGGTTCTGGAAGATA  
14487 CTGGAAGATATCGCAGTTCT  
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14494 GAGGCGTCGTTGTACATAAG  
14495 TGTACATAAGCGCCACGTCT  
14496 CGCCACGTCTGAGTTGGTGT  
14497 GAGTTGGTGTAAATCAGAAA  
30 14498 TAATCAGAAACTGGTTGGAG  
14499 CTGGTTGGAGACCCAGGAT  
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14501 GGTCCACGTCGTGGATGGCG  
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35 14503 CTTGCAAAGAGGGCAGCCAG  
14504 GGGCAGCCAGGATTCCAAG  
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14506 TCTGTGAACACAGCCTCGAG  
14507 CAGCCTCGAGGGCGGGCGTA  
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14509 GCCAGCAGCACATGCGTGGA  
14510 CATGCGTGGACTGGGCCACG  
14511 CTGGGCCACGTCGGCGGCAT  
14512 TCGGCGGCATGTAGGCTGTT  
45 14513 GTAGGCTGTTGTGGTAGGCC  
14514 GTGGTAGGCCACATTGGCGT  
14515 ACATTGGCGTGGTAGTGACC  
14516 GGTAGTGACCCTCCAGCATC  
14517 CTCCAGCATCAGCAGGTAGG  
50 14518 AGCAGGTAGGTGGCCAGTGT  
14519 TGGCCAGTGTCTGTCTGGG  
14520 GTCTGTGGGATCTGGAATG  
14521 ATCTGGAATGTCTTCAGCAG  
14522 TCTTCAGCAGGTCCCCTCC  
55 14523 GTCCCCTCCTGAAAAATGC  
14524 TGA AAAATGCTGAATATGAT  
14525 TGAATATGATAGCTGTGAGG  
14526 AGCTGTGAGGGGCGGTTCC  
14527 GGCCGGTTCCCACTTACGTC  
60 14528 CACTTACGTCCGCCACCTTG  
14529 CGCCACCTTGAACACATCAA  
14530 AACACATCAAGTCCCCACTT  
14531 GTCCCCACTTGTGGTGTCT  
14532 GTTGGTGTCTTCTAGCTCCT  
65 14533 TCTAGCTCCTTGGCCAGTTG  
14534 TGGCCAGTTGCTCCTCCTGG  
14535 CTCCTCCTGGTCACTCTGGA  
14536 TCAGTCTGGACCCCAAAGCG  
14537 CCCC AAAGCGTGGGACAGTG  
70 14538 TGGGACAGTGGCTGAGGAGA  
14539 GCTGAGGAGAGGCTGGCACT  
14540 GGCTGGCACTGTGGCAGAGC  
14541 GTGGCAGAGCCCATGTAGGC  
14542 CCATGTAGGCCACTGATCCG  
75 14543 CACTGATCCGGGACATGGGC

14544 GGACATGGGCTGTGGGGCCT  
14545 TGTGGGGCCTCCTCAGCGGT  
14546 CCTCAGCGGTACCTTGGGC  
14547 CACCTTGGGCAGCTCCACCT  
5 14548 AGCTCCACCTCGGTCTGCTG  
14549 CGGTCTGCTGGTCCAGGAAG  
14550 GTCCAGGAAGGTCCGGGAGA  
14551 GTCCGGGAGATGTA CT CGGA  
14552 TGTA CT CGGACACCTGGTTC  
10 14553 CACCTGGTTCCCGGAGCGGC  
14554 CCGGAGCGGCTGGTTTCGGA  
14555 TGGTTTCGGACAGGTGGGTC  
14556 CAGGTGGGTCAACTCCCGGT  
14557 AACTCCCGGTT CAGGATCCG  
15 14558 TCAGGATCCGCTTGA ACTTG  
14559 CTTGAACTTGTGGAGGCCA  
14560 TTGGAGGCCATCTCCCCAC  
14561 TCTCCCCACCGAGTGCCGG  
14562 CGAGTGCCGGGTCTGCAGCG  
20 14563 GTCTGCAGCGTCTCCA ACTG  
14564 TCTCCA ACTGATCCAGGCAC  
14565 ATCCAGGCACCA GTCCAGCT  
14566 CAGTCCAGCTCGTCTAGCGT  
14567 CGTCTAGCGTCTCCAATGCC  
25 14568 CTCCAATGCCAGCTTCTGCC  
14569 AGCTTCTGCCCGTGTCTCTC  
14570 CCGTGTCTCTGCAGGAGGG  
14571 TGCAGGAGGGAGCTGATTGC  
14572 AGCTGATTGCTGGATGAAGG  
30 14573 TGGATGAAGGGTTTCCGACG  
14574 GTTTCGACGGGTCCCTGCT  
14575 GGTCCCTGCTTGGCTGCTCC  
14576 TGGCTGCTCCTAGGCATTGC  
14577 TAGGCATTGCTGGCGGGCAA  
35 14578 TGGCGGGCAAGGGCCGCCAC  
14579 GGGCCGCCACGTTGCTCCGA  
14580 GTTGCTCCGAACGGTCCGCA  
14581 ACGGTCCGCAGACTGGCCAG  
14582 GACTGGCCAGGACCTGGGCA  
40 14583 GACCTGGGCAAAGGGCGTCA  
14584 AAGGGCGTCACAATCATGTC  
14585 CAATCATGTCTCTCCATGT  
14586 CTCTCCATGTAGGTCTGCTGG  
14587 AGGTGCTGGCCACAGAGGA  
45 14588 CCACAGAGGAGTTCCGAGAC  
14589 GTTCCGAGACATGGCCTTGG  
14590 ATGGCCTTGGGCGAGAGTTC  
14591 GCGAGAGTTCTAGTCGCTA  
14592 ATAGTCGCTATCTGAGCGGT  
50 14593 TCTGAGCGGTACAGGAAGGA  
14594 ACAGGAAGGACTCGCGCCGC  
14595 CTCGCGCGCTGGCTGTGCG  
14596 TGGCTGTGCGGGA CTGAGC  
14597 GGA CTGGAGCCTGCATAATC  
55 14598 CTGCATAATCCGCCCCAGGC  
14599 CGGCCAGGCCAGGGCTGGA  
14600 CAGGGCTGGA CTGAGGGTCC  
14601 CTGAGGGTCCAGGGCCCTCC  
14602 AGGGCCCTCTCCACACGA  
60 14603 TCCACACGAGAGCCCATTT  
14604 GAGCCCATTTTCCAGGTCAA  
14605 TCCAGGTCAAAGCGCCTGCA  
14606 AGCGCTGCAGGAGGAAACG  
14607 GGAGGAAACGGGCCAGGAGA  
65 14608 GGCCAGGAGAGCCGCACTT  
14609 GCCGCACTTCTGAGCTCC  
14610 CCTGAGCTCCGCGCGGGC  
14611 GGCCGCGGGCTCAGGTCCCT  
14612 TCAGGTCCCTCTCGCGCAG  
70 14613 CTCGCGGACGCCGCGGACT  
14614 CCCGCGGACTGTCCGATC  
14615 TGTCCGATCCGAATAGAAG  
14616 CGAATAGAAGCGCTGTTGGA  
14617 CGCTGTTGGATGCGGATGGG  
75 14618 TGCGGATGGGGCGCGGGGT

14619 GCGCCGGGGTTGCCGCCACA  
 14620 TGCCGCCACAGGTGCTTCGG  
 14621 GGTGCTTCGGGGCTCTGGTC  
 14622 GGCTCTGGTCATGCTGTGGC  
 5 14623 ATGCTGTGGCGGCCGCGAGA  
 14624 GGCCGCGAGAGCGACTCAAC  
 14625 GCGACTCAACCTGCTGCAAG  
 14626 CTGCTGCAAGCCTCTGCCCC  
 14627 CCTCTGCCCTTCGCGGACC  
 10 14628 TTCGCCGACCCCCAGGTTCT  
 14629 CCCAGGTTCTCCATGCGCCA  
 14630 CCATGCGCCAGAGAAAGGCT  
 14631 GAGAAAGGCTGGATGAAGGG  
 14632 GGATGAAGGGTTCCGACGG  
 15 14633 TTTCCGACGGGTCCTGCTT  
 14634 GTCCCTGCTTGGCTGCTCT  
 14635 GGCTGCTCCTAGGCATTGCT  
 14636 AGGCATTGCTGGCGGCAAG  
 14637 GGCGGCAAGGCCGCCACG  
 20 14638 GGCCGCCACGTTGCTCCGAA  
 14639 TTGCTCCGAACGGTCCGCAG

In one preferred embodiment, the links between neighboring mononucleotides are phosphodiester links. In another preferred, at least one mononucleotide phosphodiester residue of the anti-sense oligonucleotide(s) is substituted by a methylphosphonate, phosphotriester, phosphorothioate, phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, 2'-O-methyl, methylene(methyimino), methyleneoxy (methylimino), phosphoramidate residues, and combinations thereof. The oligos having one or more phosphodiester residues substituted by one or more of the other residues are generally longer lasting, given that these residues are more resistant to hydrolysis than the phosphodiester residue. In some cases up to about 10%, about 30%, about 50%, about 75%, and even all phosphodiester residues may be substituted (100%).

In another preferred embodiment, the multiple target anti-sense oligo (MTA) of the invention comprises at least about 7 mononucleotides, in some instances up to 60 and more mononucleotides, preferably about 10 to about 36, and more preferably about 12 to about 21 mononucleotides. However, other lengths are also suitable depending on the length of the target macromolecule. Examples of multi-targeted anti-sense (MTA) oligos of the invention are provided in Table 3 below, which includes ninety-four sequences (SEQ ID NOS.: 2316 through 2410).

**Table 3: MTA Oligos, Location Targeted & Target**

MTA Oligo	SEQ. ID No.	Location	Compound Targeted	Target
40 <u>HUMNEKBP65A AS</u>				
CCC GGC CCC GCC TCG TGC C	12388	5'=1	EPI 2192	
CGT CCB TGC CGC GGG CCC	12389	5'=28 (AUG)	EPI 2193	
GCC CCG CTG CTT GGG CTG CTC TGC CGG G	12390	5'=65	EPI 2194	
TCT GTG CTC CTC TCG CCT GGG	12391	5'=137	EPI 2195	
45 TGG TGG GGT GGG TCT TGG TGG	12392	5'=159	EPI 2196	
CTG TCC CTG GTC CTG TG	12393	5'=196	EPI 2197	
GGT CCC GCT TCT TC	12394	5'=362	EPI 2198	
GGG GTT GTT GTT GGT CTG G	12395	5'=401	EPI 2199	
TGT CCT CTT TCT GC	12396	5'=656	EPI 2200	
50 GCC TCG GGC CTC CC	12397	5'=697	EPI 2201	
GGC TGG GGT CTG CGT	12398	5'=769	EPI 2202	
GGC CGG GGG TCG GTG GGT CCG CTG	12399	5'=953	EPI 2203	
GGG CTG GGG TGC TGG CTT GGG G	12400	5'=1022	EPI 2204	
GGG GCT GGG GCC TGG GCC	12401	5'=1208	EPI 2205	
55 GCC TGG GTG GGC TTG GGG GC	12402	5'=1272	EPI 2206	
GCT GGG TCT GTG CTG TTG CC	12403	5'=1362	EPI 2207	
GTT GTG TGG GGG GCC	12404	5'=1451	EPI 2208	
GCT GGG TCG GGG GGC CTC TGG GCT GTC	12405	5'=1511	EPI 2209	
GCC CCG GGG CCC CC	12406	5'=1550	EPI 2210	
60 TGG CTC CCC CCT CC	12407	5'=1772	EPI 2211	
GCT CCC CCC TTT CC	12408	5'=1863	EPI 2212	
CGG ACG AAG ACA GAG A	12409	5'=1979	EPI 2213	
GGC TTT GTG GGC TC	12410	5'=2011	EPI 2214	
GCC TGC TCT CCC CC	12411	5'=2312	EPI 2215	
65 CCC GGC CCC GCC BCG BBC C	12412	intron	EPI 2192-01A	HSU50136C4Synth

	CCC GGC CCC GCC BCG	12413	intron	EPI 2192-01B	
	CCC GGC CCC GCC BCG BBC C	12414	5'untr	EPI 2192-02A	HUMLIPOX5LO
	CCC GGC CCC GCC BCG	12415	5'untr	EPI 2192-02B	
5	CCC GBC CCC GCC TCB BG	12416	trans	EPI 2192-03A	HSNFKBS Subunit
	CCC GBC CCC GCC TC	12417	trans	EPI 2192-03B	
	CCG GCC CCG CCT C	12418	5'untr	EPI 2192-04	TGFβR1
	CCC GBB CCC GCB TBG TGC C	12419	5'trans	EPI 2192-05A	HSU58198i1l enhan
	CCC GCB TBG TGC C	12420	5'untr	EPI 2192-05B	
	CCC GGB CCC BCC BBG TGC C	12421	3'trans	EPI 2192-06	HSVECAD
10	CBG BBC CCT CGT GCC	12422	intron	EPI 2192-07A	NFKB2
	C CCG CCT CGT GCC	12423	intron	EPI 2192-07B	NFKB2
	CCG GCB CCG CCT CBT GCC	12424	5'trans	EPI 2192-08	Carboxypep
	CCG GCC CCG CCB CBT GCC	12425	3'trans	EPI 2192-09	HumADRA2Ca2AdrKid
	CCC GBC CCC GBC TCG	12426	5'untrs	EPI 2192-10	HUMFK506B
15	CCC GGC CBC GBC TCG	12427	5'untrs	EPI 2192-11	HSNBARKS1βAdrKin
	CCC GGC CCB GCC TBG	12428	5'UTR	EPI 2192-12	HSNFXN1 (NFKB1)
	CCC GGC BCB GBC TCG TBC C	12429	3'UTR	EPI 2192-13	HSILF (transcrp. Factor ILF)
20	CCC GGC CCC GCC BCG	12413		EPI-2192-14	NFKB/C4Syn/5-LO/ TGFBrecl MTA
	CCC GGC CCC GCC BCG	12430		EPI-2192-15	NFKB/C4Syn/5-LOMTA
	TCC BTG CCG CGG GC	12432	3' trans	EPI-2193-01	METOncoGene
	TCC BTG CCB CGG GCC	12433	3' trans	EPI-2193-02	HSFGR2 (IG)
	TCC BTG CCB CGG GCC	12434	mid cod	EPI-2193-03	5-LO
25	TCC BTG CCB CGG GCC	12435	mid cod	EPI-2193-04	HUMTK14
	GTC CBT GBC GCG G	12436	3'trans	EPI-2193-05	HUMTNFR
	TC CBT GBC GCG GG	12437	AUG		Probl.HUMPTCH cardiacK+channel humCSPAcytotox. Ser. Protease
30	TCT GBG CTC CTC TBB CCT GGG	12438	intr	EPI-2195-01	HSINOSX08induc.NOS
	CTG TGC BCC TBB CBC CTG GG	12439	intr	EPI-2195-02	HUMACHRM2musc.m2 acetylch.rec.
	TGT GBT CCB CTB GBC TGG G	12440		EPI-2195-03	s86371s1 Neurokinin3Recept
35	TCT GTB CTC BBC TCB CCT G	12441		EPI-2195-04	HUMMIP1 Amacro Inflamm. Factor
	TGC TCC TCB CBB CTG GG	12442		EPI-2195-05	HSNBARKS4
	CTC CTC TBG CCT GG	12443		EPI-2195-06	
40	β-Adr Rec Kinase				
	GTG CTC CBB TCB BCT GGG	12444		EPI-2195-07	HSTNFR2SO6TNF R2
	GTG CBC CBB TCB CCT GGG	12445		EPI-2195-08	humfkbp fk506
	binding prot.				
	TCT GTG CBC CTC TBG BCT	12446	exon	EPI-2195-09	HSNBARKS1β-Adr. Recept.Kinase
45	CTG TBB TCC TBB CBC CTG G	12482	intron	EPI-2195-10	HUMIL8
	TGT GCT BBT CBC BCB TGG G	12448		EPI-2195-11	HSU50157 PDE4
	GTG CBC CBC TCB CCT G	12449	intron/exon	EPI-2195-12	IL-2 R
	CTG TGC BCC TCT C	12450	3'UTR	EPI-2203-05	IL-6 R HSIL6R
	CBG TGC BCC BCT CBC CTG	12451	intr/ex	EPI-2203-06A	HSIL2rG6
50	G TGC BCC BCT CBC CTG	12449	intr/ex	EPI-2203-06B	HSIL2rG6
	CBC CTC TCB CCT GGG	12453	coding	EPI-2203-07A	HUMIL71
	C CTC TCB CCT GGG	12454	coding	EPI-2203-07B	IL-7 HUMIL71
	GCT CCB CTC GCC T	12455	coding	EPI-2203-08	IL-6 R HSI6REC
	TGC TCC TCB CGC C	12456	intron PDGF A	EPI-2303-09	Chain HUMPDGFAB
55	GTT GTT GBT CTG G	12457	3'utr	EPI-2199-01	GATA-4Transcrip.
	Factor for IL-5				
	GGT TGB BBT TGG TCT TGG	12458	Coding	EPI-2199-02	TNFα HUMTNFA
	GGT TGT TGB TGB TCT G	12459	Far 5'UTR	EPI-2199-03	HSSUBP1G (Sub Pr)
	GGG TTB BBG TTG BTC TGG	12460	Coding	EPI-2199-04	NeutrophilAdh. R HUMNARIA
60	GGG TTB BBG TTG BTC TGG	12461	HSHM2	EPI-2199-05	m2 Muscarinic R
	TTG TTG TBG BTC TGG	12462	HUML1CAM	EPI-2199-06	L1 LeukAadhProt
	GGG TBG BBG BGT CCG CTG	12463	coding	EPI-2203-01	HUMGATA2A
	GGG TCB GBG GBT CBG CTG	12464	S71424S2	EPI-2203-02	IGE eps
65	GGG TBG GTG GGT C	12465	coding	EPI-2203-03	HSGCSFR2
	GGG TCG GBG GGT CBG C	12466	HUMITGF	EPI-2203-04	TGFβ3
	GGG TGG GCT T	12485	HUMNK65PRO	EPI-2206-01	NFKB/NK & TCell
70	GGG TGG GCT TGG G	12468	HUMPEREEB	EPI 2206-02	Activating Prot NFKB/Prostagl. EP3 Rec



	CCTGGGTGGGBBTGGG	12469	EPI 2206-03	HSNF2B/GCSF NFKB/GranuLocCSF/ Transcr.FactorNF2B
5	CCTGGBTGGGCBTGGG	12470	EPI-2206-04	HUMLAP/NFKB Leuk. Adhes. Prot
	GCCTGBGTGBBCTTGGG	12471	EPI2206-05	NFKB/Endothel
	N2 S63833			
	CCCAVGVCVCCAGGC	11769	EPI 2206-06	NFKBAS13/B Lymph SerThrProt.Kinase
10	AGCCACCCAGGC	11770	EPI2206-07	NFKBAS13/GCSF1 HSGCSFR1Rec
	BCCTGGGTGGGCTB	11771	EPI2206-08	NFKBAS13/GCSF1/ NK7TCELLACT. Prot
15	GGTGGGCTTGGG	11772	EPI 2206-09	NFKBAS13/
	HSTGFB1 TGFB			
	CCBGGGTGGGCTTGGG	11773	EPI 2206-10	NFKBAS13/ HSTGFB1 TGFB1
	CTGGGTGGGBBTGGG	11774	EPI 2206-11	NFKBAS13/
	HSGCSFR1 GCSFR1			
20	CCBGGGTGGGCTTGG	11775	EPI 2206-12	NFKBAS13/HUMCD30A LymphActAntigCoding
	GGGTGGGCTTGG	11776	EPI-2206-12B	NFKBAS13/HUMCD30A
	CCTGBGTGBGCBTGGG	11777	EPI 2206-13	NFKBAS13/HUMCAM1V Vasc. Endoth. Cell Adh. Molec
25				
	B: Universal Base			

The MTA oligos of Table 3 and others in accordance with this invention are suitable for use with two or more of the targets, such as those listed in Table 4 below.

**Table 4: Targets for the MTA Oligos of Table 3**

Compound	Target
EPI 2010	Adenosine A1 receptor
EPI 2045	Adenosine A3 receptor
EPI 2873, EPI 2193	NFKB
EPI 1873	Interleukin-1
EPI 1857	Interleukin -5
EPI 2945	Interleukin -4
EPI 2977	Interleukin -8
EPI 2031	5-Lipoxygenase
EPI 1898	Leukotriene C-4 Synthase
EPI 1856	Eotaxin
EPI 1131	ICAM
EPI 1085	VCAM
EPI 2085	TNF $\alpha$
EPI 1908	PAF
EPI 1925	IL-4 receptor
EPI 2643	$\beta$ 2 adrenergic receptor kinase
EPI 2934	Tryptase
EPI 2033	Major Basic Protein
EPI 2795	Eosinophil Peroxidase

Nf $\kappa$ B: nuclear factor  $\kappa$ B

ICAM: intracellular adhesion molecule

VCAM: vascular cell adhesion molecule

TNF: tumor necrosis factor

PAF: platelet activating factor

The mRNA sequence of the targeted protein or the DNA sequence of the regulatory segment may be derived from the nucleotide sequence of the gene expressing or regulating the protein, whether for existing targets or

those to be found in the future. Sequences for many target genes of different systems are presently known. See, GenBank data base, NIH, the entire sequences of which are incorporated here by reference. The sequences of those genes, whose sequences are not yet available, may be obtained by isolating the target segments applying technology known in the art. Once the sequence of the gene, its RNA and/or the protein are known, anti-sense oligonucleotides are produced as described above and utilized to validate the target by in vivo administration and testing for a reduction of the production of the targeted protein in accordance with standard techniques, and of specific functions. As already described above, the anti-sense oligonucleotides may be of any suitable length, e.g., from about 7 to about 60 nucleotides in length, depending on the particular target being bound and the mode of delivery thereof. The anti-sense oligonucleotide preferably is directed to an mRNA region containing a junction between intron and exon or to regions vicinal to the junction. Where the anti-sense oligonucleotide is directed to an intron/exon junction, it may either entirely overlie the junction or may be sufficiently close to the junction to inhibit splicing out of the intervening exon during processing of precursor mRNA to mature mRNA, e.g., with the 3' or 5' terminus of the anti-sense oligonucleotide being positioned within about, for example, 10, 5, 3, or 2 nucleotide of the intron/exon junction. Also preferred are anti-sense oligonucleotides which overlap the initiation codon and, more generally, those that target the coding region of the target mRNA. When practicing the present invention, the anti-sense oligonucleotide(s), administered, whether DNA or RNA may be related in origin to the species to which it is administered or to other species including prokaryotes. When treating humans, human anti-sense may be used if desired, except when targeting foreign invaders. Anti-sense oligos to endogenous sequences of other species, however, are also clearly encompassed.

Other agents that may be incorporated into the present composition are one or more of a variety of therapeutic agents which are administered to humans and animals. Some of the categories of agents suitable for incorporation into the present composition and formulations are analgesics, pre-menstrual medications, menopausal agents, anti-aging agents, anti-anxiolytic agents, mood disorder agents, anti-depressants, anti-bipolar mood agents, anti-schizophrenic agents, anti-cancer agents, alkaloids, blood pressure controlling agents, hormones, anti-inflammatory agents, muscle relaxants, soporific agents, anti-ischemic agents, anti-arrhythmic agents, contraceptives, vitamins, minerals, tranquilizers, neurotransmitter regulating agents, wound healing agents, anti-angiogenic agents, cytokines, growth factors, anti-metastatic agents, antacids, anti-histaminic agents, anti-bacterial agents, anti-viral agents, anti-gas agents, appetite suppressants, sun screens, emollients, skin temperature lowering products, radioactive phosphorescent and fluorescent contrast diagnostic and imaging agents, libido altering agents, bile acids, laxatives, anti-diarrheic agents, skin renewal agents, hair growth agents, analgesics, pre-menstrual medications, anti-menopausal agents such as hormones and the like, anti-aging agents, anti-anxiolytic agents, nociceptive agents, mood disorder agents, anti-depressants, anti-bipolar mood agents, anti-schizophrenic agents, anti-cancer agents, alkaloids, blood pressure controlling agents, hormones, anti-inflammatory agents, other agents suitable for the treatment and prophylaxis of diseases and conditions associated or accompanied with pain and inflammation, such as arthritis, burns, wounds, chronic bronchitis, chronic obstructive pulmonary disease (COPD), inflammatory bowel disease such as Crohn's disease and ulcerative colitis, autoimmune disease such as lupus erythematosus, muscle relaxants, steroids, soporific agents, anti-ischemic agents, anti-arrhythmic agents, contraceptives, vitamins, minerals, tranquilizers, neurotransmitter regulating agents, wound and burn healing agents, anti-angiogenic agents, cytokines, growth factors, anti-metastatic agents, antacids, anti-histaminic agents, anti-bacterial agents, anti-viral agents, anti-gas agents, agents for reperfusion injury, counteracting appetite suppressants, sun screens, emollients, skin temperature lowering products, radioactive phosphorescent and fluorescent contrast diagnostic and imaging agents, libido altering agents, bile acids, laxatives, anti-diarrheic agents, skin renewal agents, hair growth agents, etc.

Among the hormones suitable for active agents of the invention, are female and male sex hormones such as premarin, progesterone, androstenedione and their analogues, thyroxine and glucocorticoids, including Budesonide, Dexamethasone, Flunisolide, Triamcinolone, and others. Among the libido altering agents are Viagra and other NO-level modulating agents, among the analgesics are over-the-counter medications such as ibuprofen, oruda, aleve and acetaminophen and controlled substances such as morphine and codeine, among the anti-depressants are tricyclics, MAO inhibitors and epinephrine,  $\gamma$ -amino butyric acid (GABA), dopamine and serotonin level elevating agents, e.g. Prozac, Amytryptilin, Wellbutrin and Zoloft, among the skin renewal agents are Retin-A, hair growth agents such as Rogaine, among the anti-inflammatory agents are non-steroidal anti-inflammatory drugs (NSAIDs) and steroids, among the soporifics are melatonin and sleep inducing agents such as diazepam, cytoprotective, anti-ischemic and

head injury agents such as enadoline, and many others. Examples of agents in the different groups are provided in the following list. Examples of analgesics are Acetaminophen, Anilerdine, Aspirin, Buprenorphine, Butabital, Butorphanol, Choline Salicylate, Codeine, Dezocine, Diclofenac, Diflunisal, Dihydrocodeine, Elcatonin, Etodolac, Fenoprofen, Hydrocodone, Hydromorphone, Ibuprofen, Ketoprofen, Ketorolac, Levorphanol, Magnesium Salicylate, Meclofenamate, Mefenamic Acid, Meperidine, Methadone, Methotrimeprazine, Morphine, Nalbuphine, Naproxen, Opium, Oxycodone, Oxymorphone, Pentazocine, Phenobarbital, Propoxyphene, Salsalate, Sodium Salicylate, Tramadol and Narcotic analgesics in addition to those listed above. See, Mosby's Physician's GenRx. Examples of anti-anxiety agents include Alprazolam, Bromazepam, Buspirone, Chlordiazepoxide, Chlormezanone, Clorazepate, Diazepam, Halazepam, Hydroxyzine, Ketazolam, Lorazepam, Meprobamate, Oxazepam and Prazepam, among others. Examples of anti-anxiety agents associated with mental depression are Chlordiazepoxide, Amitriptyline, Loxapine, Maprotiline and Perphenazine, among others. Examples of anti-inflammatory agents are non-rheumatic Aspirin, Choline Salicylate, Diclofenac, Diflunisal, Etodolac, Fenoprofen, Fluctafenine, Flurbiprofen, Ibuprofen, Indomethacin, Ketoprofen, Magnesium Salicylate, Meclofenamate, Mefenamic Acid, Nabumetone, Naproxen, Oxaprozin, Phenylbutazone, Piroxicam, Salsalate, Sodium Salicylate, Sulindac, Tenoxicam, Tiaprofenic Acid, Tolmetin. Examples of anti-inflammatories for ocular treatment are Diclofenac, Flurbiprofen, Indomethacin, Ketorolac, Rimexolone (generally for post-operative treatment). Examples of anti-inflammatories for non-infectious nasal applications are Beclomethaxone, and the like. Examples of soporifics (anti-insomnia/sleep inducing agents) such as those utilized for treatment of insomnia, are Alprazolam, Bromazepam, Diazepam, Diphenhydramine, Doxylamine, Estazolam, Flurazepam, Halazepam, Ketazolam, Lorazepam, Nitrazepam, Prazepam, Quazepam, Temazepam, Triazolam, Zolpidem and Sopiclone, among others. Examples of sedatives are Diphenhydramine, Hydroxyzine, Methotrimeprazine, Promethazine, Propofol, Melatonin, Trimeprazine, and the like. Examples of sedatives and agents used for treatment of petit mal and tremors, among other conditions, are Amitriptyline HCl, Chlordiazepoxide, Amobarbital, Secobarbital, Aprobital, Butabarbital, Ethchlorvynol, Glutethimide, L-Tryptophan, Mephobarbital, Methohexital Na, Midazolam HCl, Oxazepam, Pentobarbital Na, Phenobarbital, Secobarbital Na, Thiamylal Na, and many others. Agents used in the treatment of head trauma (Brain Injury/Ischemia) include Enadoline HCl (e.g. for treatment of severe head injury, orphan status, Warner Lambert). Examples of cytoprotective agents and agents for the treatment of menopause and menopausal symptoms are Ergotamine, Belladonna Alkaloids and Phenobarbitals. Examples of agents for the treatment of menopausal vasomotor symptoms are Clonidine, Conjugated Estrogens and Medroxyprogesterone, Estradiol, Estradiol Cypionate, Estradiol Valerate, Estrogens, conjugated Estrogens, esterified Estrone, Estropipate and Ethinyl Estradiol. Examples of agents for treatment of symptoms of Pre Menstrual Syndrome (PMS) are Progesterone, Progestin, Gonadotrophic Releasing Hormone, oral contraceptives, Danazol, Luprolide Acetate and Vitamin B6. Examples of agents for the treatment of emotional/psychiatric treatments are Tricyclic Antidepressants including Amitriptyline HCl (Elavil), Amitriptyline HCl, Perphenazine (Triavil) and Doxepin HCl (Sinequan). Examples of tranquilizers, anti-depressants and anti-anxiety agents are Diazepam (Valium), Lorazepam (Ativan), Alprazolam (Xanax), SSRI's (selective Serotonin reuptake inhibitors), Fluoxetine HCl (Prozac), Sertaline HCl (Zoloft), Paroxetine HCl (Paxil), Fluvoxamine Maleate (Luvox), Venlafaxine HCl (Effexor), Serotonin, Serotonin Agonists (Fenfluramine), and other over the counter (OTC) medications. Examples of anti-migraine agents are Immitrex and the like.

The amount of each active agent may be adjusted when, and if, additional agents with overlapping activities are included as discussed in this patent. The dosage of the active compounds, however, may vary depending on age, weight, and condition of the subject. Treatment may be initiated with a small dosage, e.g. less than the optimal dose, of the first active agent of the invention, whether an anti-inflammatory steroid or a ubiquinone, or both, and optionally other bioactive agents described above. This may be similarly done with the second active agent, until a desirable level is attained. Or vice versa, for example in the case of multivitamins and/or minerals, the subject may be stabilized at a desired level of these products and then administered the first active compound. The dose may be increased until a desired and/or optimal effect under the circumstances is reached. In general, the active agent is preferably administered at a concentration that will afford effective results without causing any unduly harmful or deleterious side effects, and may be administered either as a single unit dose, or if desired in convenient subunits administered at suitable times throughout the day. The second therapeutic or diagnostic agent(s) is (are) administered in amounts which are known in the art to be effective for the intended application. In cases where the second agent has an overlapping activity with the principal agent, the dose of one of the other or of both agents may

be adjusted to attain a desirable effect without exceeding a dose range which avoids untoward side effects. Thus, for example, when other analgesic and anti-inflammatory agents are added to the composition, they may be added in amounts known in the art for their intended application or in doses somewhat lower than when administered by themselves.

5 Pharmaceutical compositions and kits comprising an anti-sense oligo and/or the non-corticoid steroid and/or ubiquinone including doses effective to reduce expression of target protein(s) by binding specifically with DNA or mRNA either encoding, or regulating the expression of the target proteins in the cell so as to prevent its translation are also part of the present invention. Such compositions are provided in a suitable pharmaceutically or veterinarily acceptable carrier(s), e.g., sterile pyrogen-free saline solution either separately or in combination when  
10 intended for dual administration, e.g. in a kit where both first and second agent are administered on specified dates whereas only one is administered other days. The active agents may be formulated with a hydrophobic carrier capable of passing through a cell membrane, e.g., in a liposome, with the liposomes carried in a pharmaceutically acceptable aqueous carrier. The oligonucleotides may also be coupled to a substance which inactivates mRNA, such as a ribozyme. Such oligonucleotides may be administered to a subject to inhibit the activation of a target, such as  
15 the adenosine receptors, which subject is in need of such treatment for any of the reasons discussed herein. Furthermore, the pharmaceutical formulation may also contain chimeric molecules comprising anti-sense oligonucleotides attached to molecules which are known to be internalized by cells. These oligonucleotide conjugates utilize cellular uptake pathways to increase cellular concentrations of oligonucleotides. Examples of macromolecules used in this manner include transferrin, asialoglycoprotein (bound to oligonucleotides via  
20 polylysine) and streptavidin. In the pharmaceutical formulation, the anti-sense compound may be contained within a lipid particle or vesicle, such as a liposome or microcrystal. The particles may be of any suitable structure, such as unilamellar or plurilamellar, so long as the anti-sense oligonucleotide is contained therein. Positively charged lipids such as N- [1-(2, 3 -dioleoyloxy) propyl] -N, N, N-trimethylammoniummethylsulfate, or "DOTAP," are particularly preferred for such particles and vesicles. The preparation of such lipid particles is well known. See, e.g., U.S. Patent  
25 Nos. 4,880,635 to Janoff et al.; 4,906,477 to Kurono et al.; 4,911,928 to Wallach; 4,917,951 to Wallach; 4,920,016 to Allen et al.; 4,921,757 to Wheatley et al.; etc.

The active compounds provided in this patent are preferably administered to the subject as a pharmaceutical or veterinary composition. Pharmaceutical compositions for use in the present invention include formulations suitable for systemic and topical administration, including by inhalation, intrapulmonary infusion,  
30 nasal, respirable, oral, topical (including buccal, sublingual, dermal and intraocular), parenteral (including subcutaneous, intradermal, intramuscular, intravenous and intraarticular), rectal, vaginal, ophthalmic, otical, implantable, and transdermal and iontophoretic administration, among others. The compositions may conveniently be provided in bulk, or presented in unit or multiple unit dosage form, and may be prepared by any of the methods well known in the art.

35 The first and second active compounds may be administered to the lungs, i.e. intrapulmonarily, nasally, respirably or by inhalation, of a subject by any suitable means. A preferred method of administration is by generating an aerosol or spray comprised of nasal or respirable particles comprising the active compound. The thus administered particles are then inhaled by the subject, i.e. by inhalation, intrapulmonary drip, or nasal administration, or by direct administration into the airways or respiration. The respirable particles may be liquid or  
40 solid, and they are preferably in the range of about 0.05, about 0.5, about 1, about 2, about 2.5 to about 3.5, about 4, about 6, about 8, about 10 micron, and preferably about 1 to about 5 micron (respirable or inhalable particles), or about 10, about 15, about 20, about 30 to about 50, about 100, about 150, about 200, about 300, about 400, about 500 micron, preferably about 10 to about 50, about 100 micron for intrapulmonary instillation or nasal administration. As explained above, particles of non-respirable size that are included in the aerosol or spray tend to  
45 deposit in the throat and be swallowed, and the quantity of non-respirable particles in the aerosol is preferably minimized. For nasal administration or intrapulmonary instillation, particularly for newborn babies and infants, a particle size in the range of about 10 to about 50 microns is preferred to ensure deposition and retention in the nasal or pulmonary cavity. Liquid pharmaceutical compositions of the active compound for producing an aerosol or spray may be prepared by combining the active compound with a stable vehicle, such as sterile pyrogen free water. Solid  
50 particulate compositions containing respirable dry particles of micronized active compound may be prepared by grinding dry active compound with a mortar and pestle, and then passing the micronized composition through a 400 mesh screen to break up or separate out large agglomerates. Another method would include passing through a mill

and collecting the fine particles from the device for further classification. A solid particulate composition comprised of the active compound may optionally contain a dispersant that serves to facilitate the formation of an aerosol. A suitable dispersant is lactose, which may be blended with the active compound in any suitable ratio, e. g. a 1 to 2.5 ratio by weight. Again, other therapeutic and formulation compounds may also be included, such as a surfactant to improve the state of surfactant in the lung and help with the absorption of the active agent.

The dosage of the anti-sense compound administered will depend upon the disease being treated, the condition of the subject, the particular formulation, the route of administration, the timing of administration to a subject, etc. In general, intracellular concentrations of the oligonucleotide of from about 0.01, about 0.05, about 0.1, about 0.2, about 1 to about 5  $\mu$ M, about 50  $\mu$ M, about 100  $\mu$ M or more, and more particularly about 0.2 to about 0.5  $\mu$ M, are desired. For administration to a subject such as a human, a dosage of from about 0.01, about 0.1 or about 1 mg/Kg up to about 50, about 100, or about 150 mg/Kg and even higher doses are typically employed depending on the route of administration as is known in the art. Depending on the solubility of the particular formulation of active compound administered, the daily dose may be divided among one or several unit dose administrations. Administration of the anti-sense compounds may be carried out therapeutically (i.e., as a rescue treatment) or prophylactically. Aerosols of liquid particles comprising the active compound may be produced by any suitable means, such as with a nebulizer. See, e. g. U.S. Patent No. 4,501,729. Nebulizers are commercially available devices that transform solutions or suspensions of the active ingredient into a therapeutic aerosol mist either by means of acceleration of a compressed gas, typically air or oxygen, through a narrow venturi orifice or by means of ultrasonic agitation. Suitable compositions for use in nebulizer comprise the active ingredient in a liquid carrier or diluent, the active ingredient comprising about 0.05 up to about 40% w/w of the composition, preferably about 1 to less than about 20% w/w. The carrier is typically water or a dilute aqueous alcoholic solution, preferably made isotonic with body fluids by the addition of, for example sodium chloride. Other carriers, however, are also suitable as an artisan would know. Optional additives include preservatives if the composition is not prepared sterile. An example of a preservative is methyl hydroxybenzoate, and other agents such as antioxidants, flavoring agents, volatile oils, buffering agents and surfactants, however, may also be added.

In one preferred embodiment, the pharmaceutical composition may further comprise one or more bronchodilating agents, and one or more surfactants along with a carrier and formulation agents alternatively, these active agents may be administered separately. Suitable surfactants or surfactant components for enhancing the uptake of the anti-sense oligonucleotides of the invention include synthetic and natural as well as full and truncated forms of surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D and surfactant Protein E, partially and fully saturated phosphatidylcholine (other than dipalmitoyl), dipalmitoylphosphatidylcholine, phosphatidylcholine, phosphatidylglycerol, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine; phosphatidic acid, ubiquinones, lysophosphatidylethanolamine, lysophosphatidylcholine, palmitoyl-lysophosphatidylcholine, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxyacetone, palmitate, cytidine diphosphate (CDP) diacylglycerol, CDP choline, choline, choline phosphate; as well as natural and artificial lamellar bodies which are the natural carrier vehicles for the components of surfactant, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitinic acid, non-ionic block copolymers of ethylene or propylene oxides, polyoxypropylene, monomeric and polymeric, polyoxyethylene, monomeric and polymeric, poly (vinyl amine) with dextran and/or alkanoyl side chains, Brij 35, Triton X-100 and synthetic surfactants ALEC, Exosurf, Survan and Atovaquone, among others. These surfactants may be used either as a single, or as part of a multiple component, surfactant in a formulation, or as covalently bound additions to the 5' and/or 3' ends of the anti-sense oligo(s). Aerosols of solid particles comprising the active compound may likewise be produced with any solid particulate medicament aerosol generator. Aerosol generators for administering solid particulate medicaments to a subject produce particles which are respirable, as explained above, and generate a volume of aerosol containing a predetermined metered dose of a medicament at a rate suitable for human administration. One illustrative type of solid particulate aerosol generator is an insufflator. Suitable formulations for administration by insufflation include finely comminuted powders which may be delivered by means of an insufflator or taken into the nasal cavity in the manner of a snuff. In the insufflator, the powder (e.g., a metered dose thereof effective to carry out the treatments described herein) is contained in capsules or cartridges, typically made of gelatin or foil, which are either pierced or opened in situ and the powder delivered by air drawn through the device upon inhalation or by means of a manually-operated pump. The powder employed in the insufflator consists either solely of the active ingredient or of a powder

blend comprising the active ingredient, a suitable powder diluent, such as lactose, and an optional surfactant. The active ingredient typically comprises from about 0.1 to about 100 w/w of the formulation. A second type of illustrative aerosol generator comprises a metered dose inhaler. Metered dose inhalers are pressurized aerosol dispensers, typically containing a suspension or solution formulation of the active ingredient in a liquefied propellant. During the use these devices discharge the formulation through a valve adapted to deliver a metered volume, typically from about 10:1 to about 150:1, to produce a fine particle spray containing the active ingredient. Suitable propellants include certain chlorofluorocarbon compounds, for example, dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane and mixtures thereof. The formulation may additionally contain one or more co-solvents, for example, ethanol, surfactants, such as oleic acid or sorbitan trioleate, antioxidants and suitable flavoring agents. The aerosol, whether formed from solid or liquid particles, may be produced by the aerosol generator for example at a rate of from about 10, about 30, about 70 to about 100, about 150, about 150 liters per minute, more preferably from about 30 to 150 liters per minute, and most preferably about 60 liters per minute. Aerosols containing greater amounts of medicament, however, may be administered more rapidly as is known in the art.

Aerosols of solid particles comprising the active compound may likewise be produced with any solid particulate medicament aerosol generator. Aerosol and spray generators for administering solid particulate medicaments to a subject, comprise product particles that are respirable or inhalable, and they generate a volume of aerosol containing a predetermined metered dose of a medicament at a rate suitable for human administration. Examples of such aerosol and spray generators include metered dose inhalers and insufflators known in the art. Liquid pharmaceutical compositions of active compound for producing an aerosol can be prepared by combining the anti-sense compound with the anti-inflammatory steroid(s) and/or the ubiquinone(s) and a suitable vehicle, such as sterile pyrogen free water. Other therapeutic compounds and formulation components may optionally be included as well. Solid particulate compositions containing respirable dry particles of micronized anti-sense compound may be prepared as known in the art, and generally described above, and then passing the micronized composition through a 400 mesh screen to break up or separate out large agglomerates.

Compositions suitable for oral administration may be presented in discrete units, such as capsules, cachets, lozenges, or tablets, each containing a pre-determined amount of the first and second active compounds; as a powder or granules; as a solution or a suspension in an aqueous or non-aqueous liquid; or as an oil-in-water or water-in-oil emulsion. Such compositions may be prepared by any suitable method of pharmacy that includes the step of bringing into association the active compounds and a suitable carrier. In general, the compositions of the invention are prepared by uniformly and intimately admixing the active compounds with a liquid or finely divided solid carrier, or both, and then, if necessary, shaping the resulting mixture. For example, tablet may be prepared by compressing or molding a powder or granules containing the active compound(s) alone, or optionally with one or more accessory ingredients. Compressed tablets may be prepared by compressing, in a suitable machine, the compound in a free-flowing form, such as a powder or granules optionally mixed with a binder, lubricant, inert diluent, and/or surface active/dispersing agent(s) or surfactants. Molded tablets may be made by molding, in a suitable machine, the powdered compound(s) moistened with an inert liquid binder. Compositions for oral administration may optionally include enteric coatings known in the art to prevent degradation of the compositions in the stomach and provide release of the drug in the small intestine.

Compositions suitable for buccal or sub-lingual administration include lozenges comprising the active compound in a flavored base, usually sucrose and acacia or tragacanth, and pastilles comprising the compound in an inert base such as gelatin and glycerin or sucrose and acacia.

Compositions suitable for parenteral administration comprise sterile aqueous and non-aqueous injection solutions, suspensions or emulsions of the active compound, which preparations are preferably isotonic with the blood of the intended recipient. These preparations may contain anti-oxidants, buffers, surfactants, bacteriostats, solutes which render the compositions isotonic with the blood of the intended recipient, and other formulation components known in the art. Aqueous and non-aqueous sterile suspensions may include suspending agents and thickening agents. The compositions may be presented in unit-dose or multi-dose containers, for example sealed ampoules and vials, and may be stored in a freeze-dried (lyophilized) condition requiring only the addition of the sterile liquid carrier, for example, saline or water-for-injection immediately prior to use. Extemporaneous injection solutions, suspensions and emulsions may be prepared from sterile powders, granules and tablets of the kind previously described.

Compositions suitable for topical application to the skin preferably take the form of an ointment, cream, lotion, paste, gel, spray, aerosol, or oil, although others are also suitable. Carriers that may be used include vaseline, lanoline, polyethylene glycols, alcohols, transdermal enhancers, and combinations of two or more thereof.

Compositions suitable for rectal and vaginal administration are also included and may be prepared by methods known in the art.

Compositions suitable for transdermal administration may be presented as discrete patches adapted to remain in intimate contact with the epidermis of the recipient for a prolonged period of time. Compositions suitable for transdermal administration may also be delivered by iontophoresis. See, e.g. *Pharmaceutical Research* 3:318 (1986). They typically take the form of an optionally buffered aqueous solution of the active compound containing appropriate ions to facilitate the iontophoretic delivery of the agent.

The relevant disclosures of all scientific publications and patent references cited in this patent are specifically intended to be incorporated herein by reference, particularly in reference to preparatory methods and technologies which are enabling of the invention. The following examples are provided to illustrate the present invention, and should not be construed as limiting thereon.

### EXAMPLES

In the following examples,  $\mu$ M means micromolar, ml means milliliters,  $\mu$ m means micrometers, mm means millimeters, cm means centimeters, EC means degrees Celsius,  $\mu$ g means micrograms, mg means milligrams, g means grams, kg means kilograms, M means molar, and h or hr. means hours.

#### Example 1: Design and Synthesis of Anti-sense Oligonucleotides

The design of anti-sense oligonucleotides against the  $A_1$  and  $A_3$  adenosine receptors may require the solution of the complex secondary structure of the target  $A_1$  receptor mRNA and the target  $A_3$  receptor mRNA. After generating this structure, anti-sense nucleotide are designed which target regions of mRNA which might be construed to confer functional activity or stability to the mRNA and which optimally may overlap the initiation codon. Other target sites are readily usable. As a demonstration of specificity of the anti-sense effect, other oligonucleotides not totally complementary to the target mRNA, but containing identical nucleotide compositions on a w/w basis, are included as controls in anti-sense experiments.

The mRNA secondary structure of the adenosine  $A_1$  receptor was analyzed and used as described above, to design a phosphorothioate anti-sense oligonucleotide. The anti-sense oligonucleotide which was synthesized was designated HAdA<sub>1</sub>AS and had the following sequence: 5' -GAT GGA GGG CGG CAT GGC GGG-3' (SEQ ID NO:9370). As a control, a mismatched phosphorothioate anti-sense nucleotide designated HAdA1MM1 was synthesized with the following sequence: 5' -GTA GCA GGC GGG GAT GGG GGC-3' (SEQ ID NO:9371). Each oligonucleotide had identical base content and general sequence structure. Homology searches in GENBANK (release 85.0) and EMBL (release 40.0) indicated that the anti-sense oligonucleotide was specific for the human and rabbit adenosine  $A_1$  receptor genes, and that the mismatched control was not a candidate for hybridization with any known gene sequence.

The secondary structure of the adenosine  $A_3$  receptor mRNA was similarly analyzed and used as described above to design two phosphorothioate anti-sense oligonucleotides. The first anti-sense oligonucleotide (HAdA<sub>3</sub>AS1) synthesized had the following sequence: 5' -GTT GTT GGG CAT CTT GCC-3' (SEQ ID NO:9372). As a control, a mismatched phosphorothioate anti-sense oligonucleotide (HAdA<sub>3</sub>MM1) was synthesized, having the following sequence: 5' -GTA CTT GCG GAT CTA GGC-3' (SEQ ID NO:9373). A second phosphorothioate anti-sense oligonucleotide (HAdA<sub>3</sub>AS2) was also designed and synthesized, having the following sequence: 5' -GTG GGC CTA GCT CTC GCC-3' (SEQ ID NO:9374). Its control oligonucleotide (HAdA<sub>3</sub>MM2) had the sequence: 5' -GTC GGG GTA CCT GTC GGC-3' (SEQ ID NO:9375). Phosphorothioate oligonucleotides were synthesized on an Applied Biosystems Model 396 Oligonucleotide Synthesizer, and purified using NENSORB chromatography (DuPont, MD).

#### Example 2: In Vivo Testing of Adenosine $A_1$ Receptor Anti-sense Oligos

The anti-sense oligonucleotide against the human  $A_1$  receptor (SEQ ID NO:9370) described above, was tested for efficacy in an in vitro model utilizing lung adenocarcinoma cells HTB-54. HTB-54 lung adenocarcinoma cells were demonstrated to express the  $A_1$  adenosine receptor using standard northern blotting procedures and



receptor probes designed and synthesized in the laboratory.

HTB-54 human lung adenocarcinoma cells (106/100 mm tissue culture dish) were exposed to 5.0 :M HAdA1AS or HAdAIMM1 for 24 hours, with a fresh change of media and oligonucleotides after 12 hours of incubation. Following 24 hour exposure to the oligonucleotides, cells were harvested and their RNA extracted by standard procedures. A 21-mer probe corresponding to the region of mRNA targeted by the anti-sense (and therefore having the same sequence as the anti-sense, but not phosphorothioated) was synthesized and used to probe northern blots of RNA prepared from HAdA1AS-treated, HAdAIMM1-treated and non-treated HTB-54 cells. These blots showed clearly that HAdA1AS but not HAdAIMM1 effectively reduced human adenosine receptor mRNA by >50%. This result showed that HAdA1AS is a good candidate for an anti-asthma drug since it depletes intracellular mRNA for the adenosine A<sub>1</sub> receptor, which is involved in asthma.

**Example 3: In Vivo Efficacy of Adenosine A<sub>1</sub> Receptor Anti-sense Oligos**

A fortuitous homology between the rabbit and human DNA sequences within the adenosine A<sub>1</sub> gene overlapping the initiation codon permitted the use of the phosphorothioate anti-sense oligonucleotides initially designed for use against the human adenosine A<sub>1</sub> receptor in a rabbit model. Neonatal New Zealand white Pasteurella-free rabbits were immunized intraperitoneally within 24 hours of birth with 312 antigen units/ml house dust mite (*D. farinae*) extract (Berkeley Biologicals, Berkeley, CA), mixed with 10% kaolin. Immunizations were repeated weekly for the first month and then biweekly for the next 2 months. At 3-4 months of age, eight sensitized rabbits were anesthetized and relaxed with a mixture of ketamine hydrochloride (44 mg/kg) and acepromazine maleate (0.4 mg/kg) administered intramuscularly. The rabbits were then laid supine in a comfortable position on a small molded, padded animal board and intubated with a 4.0-mm intratracheal tube (Mallinkrodt, Inc., Glens Falls, NY). A polyethylene catheter of external diameter 2.4 mm with an attached latex balloon was passed into the esophagus and maintained at the same distance (approximately 16 cm) from the mouth throughout the experiments. The intratracheal tube was attached to a heated Fleisch pneumotachograph (size 00; DOM Medical, Richmond, VA), and flow was measured using a Validyne differential pressure transducer (Model DP-45161927; Validyne Engineering Corp., Northridge, CA) driven by a Gould carrier amplifier (Model 11-4113; Gould Electronic, Cleveland, OH). The esophageal balloon was attached to one side of the differential pressure transducer, and the outflow of the intratracheal tube was connected to the opposite side of the pressure transducer to allow recording of transpulmonary pressure. Flow was integrated to give a continuous tidal volume, and measurements of total lung resistance (RL) and dynamic compliance (C<sub>dyn</sub>) were calculated at isovolumetric and flow zero points, respectively, using an automated respiratory analyzer (Model 6; Buxco, Sharon, CT). Animals were randomized and on Day 1 pretreatment values for PC<sub>50</sub> were obtained for aerosolized adenosine. Anti-sense (HAdA1AS) or mismatched control (HAdAIMM) oligonucleotides were dissolved in sterile physiological saline at a concentration of 5000 µg (5 mg) per 1.0 ml. Animals were subsequently administered the aerosolized anti-sense or mismatch oligonucleotide via the intratracheal tube (approximately 5000 :g in a volume of 1.0 ml), twice daily for two days. Aerosols of either saline, adenosine, or anti-sense or mismatch oligonucleotides were generated by an ultrasonic nebulizer (DeVilbiss, Somerset, PA), producing aerosol droplets 80% of which were smaller than 5 :m in diameter. In the first arm of the experiment, four randomly selected allergic rabbits were administered anti-sense oligonucleotide and four the mismatched control oligonucleotide. On the morning of the third day, PC<sub>50</sub> values (the concentration of aerosolized adenosine in mg/ml required to reduce the dynamic compliance of the bronchial airway 50% from the baseline value) were obtained and compared to PC<sub>50</sub> values obtained for these animals prior to exposure to oligonucleotide. Following a 1 week interval, animals were crossed over, with those previously administered mismatch control oligonucleotide now administered anti-sense oligonucleotide, and those previously treated with anti-sense oligonucleotide now administered mismatch control oligonucleotide. Treatment methods and measurements were identical to those employed in the first arm of the experiment. It should be noted that in six of the eight animals treated with anti-sense oligonucleotide, adenosine-mediated bronchoconstriction could not be obtained up to the limit of solubility of adenosine, 20 mg/ml. For the purpose of calculation, PC<sub>50</sub> values for these animals were set at 20 mg/ml. The values given therefore represent a minimum figure for anti-sense effectiveness. Actual effectiveness was higher. The results of this experiment are illustrated in Table 5 below.

**Table 5: Effect of Adenosine A<sub>1</sub> Receptor Anti-sense Oligo upon PC<sub>50</sub> Values in Asthmatic Rabbits**

Mismatch Control		A <sub>1</sub> Receptor Anti-sense Oligo	
Pre Oligonucleotide	Post Oligonucleotide	Pre Oligonucleotide	Post Oligonucleotide
3.56 ± 1.02	5.16 ± 1.03	2.36 ± 0.68	>19.5 ± 0.34**

The results are presented as the mean (n=8) ± SEM.

The significance was determined by repeated-measures analysis of variance (ANOVA), and Tukey's protected test.

\*\*Significantly different from all other groups, p<0.01.

In both arms of the experiment, animals receiving the anti-sense oligonucleotide showed an order of magnitude increase in the dose of aerosolized adenosine required to reduce dynamic compliance of the lung by 50%. No effect of the mismatched control oligonucleotide upon PC<sub>50</sub> values was observed. No toxicity was observed in any animal receiving either anti-sense or control inhaled oligonucleotide. These results show clearly that the lung has exceptional potential as a target for anti-sense oligonucleotide-based therapeutic intervention in lung disease. They further show, in a model system which closely resembles human asthma, that downregulation of the adenosine A<sub>1</sub> receptor largely eliminates adenosine-mediated bronchoconstriction in asthmatic airways. Bronchial hyperresponsiveness in the allergic rabbit model of human asthma is an excellent endpoint for anti-sense intervention since the tissues involved in this response lie near to the point of contact with aerosolized oligonucleotides, and the model closely simulates an important human disease.

**Example 4: Specificity of A<sub>1</sub>-adenosine Receptor Anti-sense Oligonucleotide**

At the conclusion of the cross-over experiment of Example 3 above, airway smooth muscle from all rabbits was quantitatively analyzed for adenosine A<sub>1</sub> receptor number. As a control for the specificity of the anti-sense oligonucleotide, adenosine A<sub>2</sub> receptors, which should not have been affected, were also quantified. Airway smooth muscle tissue was dissected from each rabbit and a membrane fraction prepared according to the method of Kleinstein et al. (Kleinstein, J. and Glossmann, H., Naunyn-Schmiedeberg's Arch. Pharmacol. 305: 191-200 (1978)), the relevant portion of which is hereby incorporated in its entirety by reference, with slight modifications. Crude plasma membrane preparations were stored at -70EC until the time of assay. Protein content was determined by the method of Bradford (M. Bradford, Anal. Biochem. 72, 240-254 (1976), the relevant portion of which is hereby incorporated in its entirety by reference). Frozen plasma membranes were thawed at room temperature and were incubated with 0.2 U/ml adenosine deaminase for 30 minutes at 37EC to remove endogenous adenosine. The binding of [<sup>3</sup>H] DPCPX (A<sub>1</sub> receptor-specific) or [<sup>3</sup>H] CGS-21680 (A<sub>1</sub> receptor-specific) was measured as previously described by Ali et al. (Ali, S. et al., J. Pharmacol. Exp. Ther. 268, Am. J. Physiol 266, L271-277 (1994), the relevant portion of which is hereby incorporated in its entirety by reference). The animals treated with adenosine A<sub>1</sub> anti-sense oligonucleotide in the cross-over experiment had a nearly 75% decrease in A<sub>1</sub> receptor number compared to controls, as assayed by specific binding of the A<sub>1</sub>-specific antagonist DPCPX. There was no change in adenosine A<sub>2</sub> receptor number, as assayed by specific binding of the A<sub>2</sub> receptor-specific agonist 2- [p- (2-carboxyethyl)-phenethylamino] -5' - (N-ethylcarboxamido) adenosine (CGS-21680). This is illustrated in Table 6 below.

**Table 6: Specificity of Action of Adenosine A<sub>1</sub> Receptor Oligonucleotide Anti-sense**

Mismatch Control Oligonucleotide	A <sub>1</sub> Anti-sense Oligonucleotide	
A <sub>1</sub> -Specific Binding	1105 ± 48**	293 ± 18
A <sub>2</sub> -Specific Binding	302 ± 22	442 ± 171

The results are presented as the mean (n = 8) ± SEM.

The significance was determined by repeated-measures analysis of variance (ANOVA), and Tukey's protected test.

\*\*Significantly different from mismatch control, p<0.01.

The above results illustrate the effectiveness of anti-sense oligonucleotides in treating airway disease. Since the anti-sense oligos described above, eliminate the receptor systems responsible for adenosine-mediated bronchoconstriction, it may be less imperative to eliminate adenosine from them. However, it would be preferable to eliminate adenosine from even these oligonucleotides to reduce the dose needed to attain a similar effect. Described

above are other anti-sense oligonucleotides targeting mRNA of proteins involved in inflammation. Adenosine has been eliminated from their nucleotide content to prevent its liberation during degradation.

**Example 5: Anti-sense Oligos directed to other Target Nucleic Acids**

This work was conducted to demonstrate that the present invention is broadly applicable to anti-sense oligonucleotides ("oligos") specific to nucleic acid targets broadly. The following experimental studies were conducted to show that the method of the invention is broadly suitable for use with anti-sense oligos designed as taught by this application and targeted to any and all adenosine receptor mRNAs. For this purpose, various anti-sense oligos were prepared to adenosine receptor mRNAs exemplified by the adenosine A<sub>1</sub>, A<sub>2b</sub> and A<sub>3</sub> receptor mRNAs. Anti-sense Oligo I was disclosed above (SEQ ID NO:9370). Five additional anti-sense phosphorothioate oligos were designed and synthesized as indicated above.

- 1- Oligo II (SEQ ID NO: 9376) also targeted to the adenosine A<sub>1</sub> receptor, but to a different region than Oligo I.
- 2- Oligo V (SEQ ID NO: 9379) targeted to the adenosine A<sub>2b</sub> receptor.
- 3- Oligos III (SEQ ID NO: 9377) and IV (SEQ ID NO: 9378) targeted to different regions of the adenosine A<sub>3</sub> receptor.
- 4- Oligo I-PD (SEQ ID NO: 11050) (a phosphodiester oligo of the same sequence as Oligo I).

These anti-sense oligos were designed for therapy on a selected species as described above and are generally specific for that species, unless the segment of the target mRNA of other species happens to contain a similar sequences. All anti-sense oligos were prepared as described below, and tested in vivo in a rabbit model for bronchoconstriction, inflammation and allergy, which have breathing difficulties and impeded lung airways, as is the case in ailments such as asthma, as described in the above-identified application.

**Example 6: Design & Sequences of other Anti-sense Oligos**

Six oligos and their effects in a rabbit model were studied and the results of these studies are reported and discussed below. Five of these oligos were selected for this study to complement the data on Oligo I (SEQ ID NO: 9370) provided in Examples 1 to 4 above. This oligo is anti-sense to one region of the adenosine A<sub>1</sub> receptor mRNA. The oligos tested are identified as anti-sense Oligos I (SEQ ID NO: 9370) and II (SEQ ID NO: 9376) targeted to a different region of the adenosine A<sub>1</sub> receptor mRNA, Oligo V (SEQ ID NO:9377) targeted to the adenosine A<sub>2b</sub> receptor mRNA, and anti-sense Oligos III and IV (SEQ ID NOS: 9378 and 9379) targeted to two different regions of the adenosine A<sub>3</sub> receptor mRNA. The sixth oligo (Oligo I-PD) is a phosphodiester version of Oligo I (SEQ ID NO:9370). The design and synthesis of these anti-sense oligos was performed in accordance with Example 1 above.

**(I) Anti-sense Oligo I**

The anti-sense oligonucleotide I referred to in Examples 1 to 4 above is targeted to the human A<sub>1</sub> adenosine receptor mRNA (EPI 2010). Anti-sense oligo I is 21 nucleotide long, overlaps the initiation codon, and has the following sequence: 5'-GAT GGA GGG CGG CAT GGC GGG-3' (SEQ ID NO:9370). The oligo I was previously shown to abrogate the adenosine-induced bronchoconstriction in allergic rabbits, and to reduce allergen-induced airway obstruction and bronchial hyperresponsiveness (BHR), as discussed above and shown by Nyce, J. W. & Metzger, W. J., Nature, 385:721 (1977), the relevant portions of which reference are incorporated in their entireties herein by reference.

**(II) Anti-sense Oligo II**

A phosphorothioate anti-sense oligo (SEQ ID NO:9376) was designed in accordance with the invention to target the rabbit adenosine A<sub>1</sub> receptor mRNA region +936 to +956 relative to the initiation codon (start site). The anti-sense oligo II is 21 nucleotide long, and has the following sequence: 5'-CTC GTC GCC GTC GCC GGC GGG-3' (SEQ ID NO:9376).

**(III) Anti-sense Oligo III**

A phosphorothioate anti-sense oligo other than that provided in Example 1 above (SEQ ID NO:9377) was designed in accordance with the invention to target the anti-sense A<sub>3</sub> receptor mRNA region +3 to +22 relative to the initiation codon start site. The anti-sense oligo III is 20 nucleotide long, and has the following sequence: 5'-GGG TGG TGC TAT TGT CGG GC-3' (SEQ ID NO:9377).

**(IV) Anti-sense Oligo IV**

Yet another phosphorothioate anti-sense oligo (SEQ ID NO:9378) was designed in accordance with the invention to target the adenosine A<sub>3</sub> receptor mRNA region +386 to +401 relative to the initiation codon (start site). The anti-sense oligo IV is 15 nucleotide long, and has the following sequence: 5'-GGC CCA GGC CCA

**GCC-3' (SEQ ID NO:9378)****(V) Anti-sense Oligo V**

A phosphorothioate anti-sense oligo (SEQ ID NO:9379) was designed in accordance with the invention to target the adenosine A<sub>2b</sub> receptor mRNA region -21 to -1 relative to the initiation codon (start site). The anti-sense oligonucleotide V is 21 nucleotide long, and has the following sequence: 5'-GGC CGG GCC AGC CGG GCC CGG-3' (SEQ ID NO:9379).

**(VI) A<sub>1</sub> Mismatch Oligos**

Two different mismatched oligonucleotides having the following sequences were used as controls for anti-sense oligo I (SEQ ID NO: 1) described in Example 5 above: A<sub>1</sub> MM2:5'-GTA GGT GGC GGG CAA GGC GGG-3' (SEQ ID NO:12490), and A<sub>1</sub> MM3:5'-GAT GGA GGC GGC CAT GGC GGG-3' (SEQ ID NO:12489). Anti-sense oligo I and the two mismatch anti-sense oligos had identical base content and general sequence structure. Homology searches in GENBANK (release 85.0) and EMBL (release 40.0) indicated that the anti-sense oligo I was specific, not only for the human, but also for the rabbit, adenosine A<sub>1</sub> receptor genes, and that the mismatched controls were not candidates for hybridization with any known human or animal gene sequence.

**(VII) Anti-sense Oligo A<sub>1</sub>-PD (Oligo VI)**

A phosphodiester anti-sense oligo (Oligo VI; SEQ ID NO:9370) having the same nucleotide sequence as Oligo I was designed as disclosed in the above-identified application. Anti-sense oligo I-PD is 21 nucleotide long, overlaps the initiation codon, and has the following sequence: 5'- GAT GGA GGC CGG CAT GGC GGG-3' (SEQ ID NO:9370).

**(III) Controls**

Each rabbit was administered 5.0 ml aerosolized sterile saline following the same schedule as for the anti-sense oligos in (II), (III), and (IV) above.

**Example 7: Synthesis of Anti-sense Oligos**

Phosphorothioate anti-sense oligos having the sequences described in (a) above, were synthesized on an Applied Biosystems Model 396 Oligonucleotide Synthesizer, and purified using NENSORB chromatography (DuPont, DE). TETD (tetraethylthiuram disulfide) was used as the sulfurizing agent during the synthesis. Anti-sense oligonucleotide II (SEQ ID NO:9376), anti-sense oligonucleotide III (SEQ ID NO: 9377) and anti-sense oligonucleotide IV (SEQ ID NO: 9378) were each synthesized and purified in this manner.

**Example 8: Preparation of Allergic Rabbits**

Neonatal New Zealand white Pasturella-free rabbits were immunized intraperitoneally within 24 hours of birth with 0.5 ml of 312 antigen units/ml house dust mite (*D. farinae*) extract (Berkeley Biologicals, Berkeley, CA) mixed with 10% kaolin as previously described (Metzger, W. J., in Late Phase Allergic Reactions, Dorsch, W., Ed., CRC Handbook, pp. 347-362, CRC Press, Boca Raton (1990); Ali, S., Metzger, W. J. and Mustafa, S. J., Am. J. Resp. Crit. Care Med. 149: 908 (1994)), the relevant portions of which are incorporated in their entireties here by reference. Immunizations were repeated weekly for the first month and then biweekly until the age of 4 months. These rabbits preferentially produce allergen-specific IgE antibody, typically respond to aeroallergen challenge with both an early and late-phase asthmatic response, and show bronchial hyper responsiveness (BHR). Monthly intraperitoneal administration of allergen (312 units dust mite allergen, as above) continues to stimulate and maintain allergen-specific IgE antibody and BHR. At 4 months of age, sensitized rabbits were prepared for aerosol administration as described by Ali et al. (Ali, S., Metzger, W. J. and Mustafa, S. J., Am. J. Resp. Crit. Care Med. 149 (1994)), the relevant section being incorporated in its entirety here by reference.

**DOSE-RESPONSE STUDIES****Example 9: Experimental Setup**

Aerosols of either adenosine (0-20 mg/ml), or anti-sense or one of two mismatch oligonucleotides (5 mg/ml) were separately prepared with an ultrasonic nebulizer (Model 646, DeVilbiss, Somerset, PA), which produced aerosol droplets, 80% of which were smaller than 5 μm in diameter. Equal volumes of the aerosols were administered directly to the lungs via an intratracheal tube. The animals were randomized, and administered aerosolized adenosine. Day 1 pre-treatment values for sensitivity to adenosine were calculated as the dose of adenosine causing a 50% loss of compliance (PC<sub>50</sub> Adenosine). The animals were then administered either the aerosolized anti-sense or one of the mismatch anti-sense oligos via the intratracheal tube (5 mg/1.0 ml), for 2 minutes, twice daily for 2

days (total dose, 20 mg). Post-treatment PC<sub>50</sub> values were recorded (post-treatment challenge) on the morning of the third day. The results of these studies are provided in Example 21 below.

#### **Example 10: Crossover Experiments**

For some experiments utilizing anti-sense oligo I (SEQ ID NO: 9370) and a corresponding mismatch control oligonucleotide A<sub>1</sub>MM2, following a 2 week interval, the animals were crossed over, with those previously administered the mismatch control A<sub>1</sub>MM2, now receiving the anti-sense oligo I, and those previously treated with the anti-sense oligo I, now receiving the mismatch control A<sub>1</sub>MM2 oligo. The number of animals per group was as follows. For mismatch A<sub>1</sub>MM2 (Control 1), n=7, since one animal was lost in the second control arm of the experiment due to technical difficulties, for mismatch A<sub>1</sub>MM3 n=4 (Control 2) and for A<sub>1</sub>AS anti-sense oligo I, n=8. The A<sub>1</sub>MM3 oligo-treated animals were analyzed separately and were not part of the cross-over experiment. The treatment methods and measurements employed following the cross-over were identical to those employed in the first arm of the experiment. In 6 of the 8 animals treated with the anti-sense oligo I (SEQ ID NO: 9370), no PC<sub>50</sub> value could be obtained for adenosine doses of up to 20 mg/ml, which is the limit of solubility of adenosine. Accordingly, the PC<sub>50</sub> values for these animals were assumed to be 20 mg/ml for calculation purposes. The values given, therefore, represent a minimum figure for the effectiveness of the anti-sense oligonucleotides of the invention. Other groups of allergic rabbits (n=4 for each group) were administered 0.5 or 0.05 mg doses of the anti-sense oligo I (SEQ ID NO: 9370), or the A<sub>1</sub>MM2 oligo in the manner and according to the schedule described above (the total doses being 2.0 or 0.2 mg). The results of these studies are provided in Example 22 below.

#### **Example 11: Anti-sense Oligo Formulation**

Each one of anti-sense oligos were separately solubilized in an aqueous solution and administered as described for anti-sense oligo I (SEQ ID NO: 9370) in (e) above, in four 5 mg aliquots (20 mg total dose) by means of a nebulizer via endotracheal tube, as described above. The results obtained for anti-sense oligo I and its mismatch controls confirmed that the mismatch controls are equivalent to saline, as described in Example 19 below and in Table 1 of Nyce & Metzger, Nature 385: 721-725 (1997). Because of this finding, saline was used as a control for pulmonary function studies employing anti-sense oligos II, III and IV (SEQ ID NO: 9376, 9377 and 9378).

#### **Example 12: Specificity of Oligo I for Adenosine A<sub>1</sub> Receptor (Receptor Binding Studies)**

Tissue from airway smooth muscle was dissected to primary, secondary and tertiary bronchi from rabbits which had been administered 20 mg oligo I (SEQ ID NO: 9370) in 4 divided doses over a period of 48 hours as described above. A membrane fraction was prepared according to the method of Ali et al. (Ali, S., et al., Am. J. Resp. Crit. Care Med. 149: 908 (1994), the relevant section relating to the preparation of the membrane fraction is incorporated in its entirety hereby by reference). The protein content was determined by the method of Bradford and plasma membranes were incubated with 0.2 U/ml adenosine deaminase for 30 minutes at 37°C to remove endogenous adenosine. See, Bradford, M. M. Anal. Biochem. 72, 240-254 (1976), the relevant portion of which is hereby incorporated in its entirety by reference. The binding of [<sup>3</sup>H]DPCPX, [<sup>3</sup>H]NPC17731, or [<sup>3</sup>H]CGS-21680 was measured as described by Jarvis et al. See, Jarvis, M.F., et al., Pharmacol. Exptl. Ther. 251, 888-893 (1989), the relevant portion of which is fully incorporated herein by reference. The results of this study are shown in Table 8 and discussed in Example 20 below.

#### **Example 13: Pulmonary Function Measurements (Compliance c<sub>DYN</sub> and Resistance)**

At 4 months of age, the immunized animals were anesthetized and relaxed with 1.5 ml of a mixture of ketamine HCl (35 mg/kg) and acepromazine maleate (1.5 mg/kg) administered intramuscularly. After induction of anesthesia, allergic rabbits were comfortably positioned supine on a soft molded animal board. Salve was applied to the eyes to prevent drying, and they were closed. The animals were then intubated with a 4.0 mm intermediate high-low cuffed Murphy 1 endotracheal tube (Mallinckrodt, Glen Falls, NY), as previously described by Zavala and Rhodes. See, Zavala and Rhodes, Proc. Soc. Exp. Biol. Med. 144: 509-512 (1973), the relevant portion of which is incorporated herein by reference in its entirety. A polyethylene catheter of OD 2.4 mm (Becton Dickinson, Clay Adams, Parsippany NJ) with an attached thin-walled latex balloon was passed into the esophagus and maintained at the same distance (approximately 16 cm) from the mouth throughout the experiment. The endotracheal tube was attached to a heated Fleisch pneumotach (size 00; DEM Medical, Richmond, VA), and the flow (v) measured using

a Validyne differential pressure transducer (Model DP-45-16-1927, Validyne Engineering, Northridge, CA), driven by a Gould carrier amplifier (Model 11-4113, Gould Electronics, Cleveland, OH). An esophageal balloon was attached to one side of the Validyne differential pressure transducer, and the other side was attached to the outflow of the endotracheal tube to obtain transpulmonary pressure ( $P_p$ ). The flow was integrated to yield a continuous tidal volume, and the measurements of total lung resistance ( $R_t$ ) and dynamic compliance ( $C_{dyn}$ ) were made at isovolumetric and zero flow points. The flow, volume and pressure were recorded on an eight channel Gould 2000 W high-frequency recorder and  $C_{dyn}$  was calculated using the total volume and the difference in  $P_p$  at zero flow, and  $R_t$  was calculated as the ratio of  $P_{tp}$  and  $V$  at midtidal lung volumes. These calculations were made automatically with the Buxco automated pulmonary mechanics respiratory analyzer (Model 6, Buxco Electronics, Sharon, CT), as previously described by Giles et al. See, Giles et al., Arch. Int. Pharmacodyn. Ther. 194: 213-232 (1971), the relevant portion of which describing these calculations is incorporated in toto hereby by reference. The results obtained upon administration of oligo II on allergic rabbits are shown and discussed in Example 26 below.

**Example 14: Measurement of Bronchial Hyperresponsiveness (BHR)**

Each allergic rabbit was administered histamine by aerosol to determine their baseline hyperresponsiveness. Aerosols of either saline or histamine were generated using a DeVilbiss nebulizer (DeVilbiss, Somerset, PA) for 30 seconds and then for 2 minutes at each dose employed. The ultrasonic nebulizer produced aerosol droplets of which 80% were <5 micron in diameter. The histamine aerosol was administered in increasing concentrations (0.156 to 80 mg/ml) and measurements of pulmonary function were made after each dose. The B4R was then determined by calculating the concentration of histamine (mg/ml) required to reduce the  $C_{dyn}$  50% from baseline ( $PC_{50}$  Histamine).

**Example 15: Cardiovascular Effect of Anti-sense Oligo I**

The measurement of cardiac output and other cardiovascular parameters using CardiomaxJ utilizes the principal of thermal dilution in which the change in temperature of the blood exiting the heart after a venous injection of a known volume of cool saline is monitored. A single rapid injection of cool saline was made into the right atrium via cannulation of the right jugular vein, and the corresponding changes in temperature of the mixed injectate and blood in the aortic arch were recorded via cannulation of the carotid artery by a temperature-sensing miniprobe. Twelve hours after the allergic rabbits had been treated with aerosols of oligo I (EPI 2010; SEQ ID NO: 9370) as described in (d) above, the animals were anesthetized with 0.3 ml/kg of 80% Ketamine and 20% Xylazine. This time point coincides with previous data showing efficacy for SEQ ID NO: 9370, as is clearly shown by Nyce & Metzger, (1997), supra, the pertinent disclosure being incorporated in its entirety here by reference. A thermocouple was then inserted into the left carotid artery of each rabbit, and was then advanced 6.5 cm and secured with a silk ligature. The right jugular vein was then cannulated and a length of polyethylene tubing was inserted and secured. A thermodilution curve was then established on a CardiomaxJ II (Columbus Instruments, Ohio) by injecting sterile saline at 20EC to determine the correctness of positioning of the thermocouple probe. After establishing the correctness of the position of the thermocouple, the femoral artery and vein were isolated. The femoral vein was used as a portal for drug injections, and the femoral artery for blood pressure and heart rate measurements. Once constant baseline cardiovascular parameters were established, CardiomaxJ measurements of blood pressure, heart rate, cardiac output, total peripheral resistance, and cardiac contractility were made.

**Example 16: Duration of Action of Oligo I (SEQ ID NO: 9370)**

Eight allergic rabbits received initially increasing log doses of adenosine by means of a nebulizer via an intra-tracheal tube as described in (f) above, beginning with 0.156 mg/ml until compliance was reduced by 50% ( $PC_{50}$  Adenosine) to establish a baseline. Six of the rabbits then received four 5 mg aerosolized doses of (SEQ ID NO: 9370) as described above. Two rabbits received equivalent amounts of saline vehicle as controls. Beginning 18 hours after the last treatment, the  $PC_{50}$  Adenosine values were tested again. After this point, the measurements were continued for all animals each day, for up to 10 days. The results of this study are discussed in Example 25 below.

**Example 17: Reduction of Adenosine  $A_{2b}$  Receptor Number by Anti-sense Oligo V**

Sprague Dawley rats were administered 2.0 mg respirable anti-sense oligo V (SEQ ID NO:9379) three times over two days using an inhalation chamber as described above. Twelve hours after the last administration, lung parenchymal tissue was dissected and assayed for adenosine  $A_{2b}$  receptor binding using [311]-NECA as described by Nyce & Metzger (1997), supra. Controls were conducted by administration of equal volumes of saline.

The results are significant at  $p < 0.05$  using Student's paired  $t$  test, and are discussed in Example 28 below.

**Example 18: Comparison of Oligo I & Corresponding  
Phosphodiester Oligo VI (SEQ ID NO:11050)**

Oligo I (SEQ ID NO:9370) countered the effects of adenosine and eliminated sensitivity to it for adenosine amount up to 20 mg adenosine/5.0 ml (the limit of solubility of adenosine). Oligo VI (SEQ ID NO: 11050), the phosphodiester version of the oligonucleotide sequence, was completely ineffective when tested in the same manner. Both compounds have identical sequence, differing only in the presence of phosphorothioate residues in Oligo I (SEQ ID NO:9370), and were delivered as an aerosol as described above and in Nyce & Metzger (1997), *supra*. Significantly different at  $p < 0.001$ , Student's paired  $t$  test. The results are discussed in Example 29 below.

**RESULTS OBTAINED FOR ANTI-SENSE OLIGO I (SEQ ID NO: 1)**

**Example 19: Results of Prior Work**

The nucleotide sequence and other data for anti-sense oligo I (SEQ ID NO: 9370), which is specific for the adenosine A<sub>1</sub> receptor, were provided above. The experimental data showing the effectiveness of oligo I in down regulating the receptor number and activity were also provided above. Further information on the characteristics and activities of anti-sense oligo I is provided in Nyce, J. W. and Metzger, W. J., *Nature* 385:721 (1997), the relevant parts of which relating to the following results are incorporated in their entireties herein by reference. The Nyce & Metzger (1997) publication provided data showing that the anti-sense oligo I (SEQ ID NO: 9370):

(1) The anti-sense oligo I reduces the number of adenosine A<sub>1</sub> receptors in the bronchial smooth muscle of allergic rabbits in a dose-dependent manner as may be seen in Table 5 below.

(2) Anti-sense Oligo I attenuates adenosine-induced bronchoconstriction and allergen-induced bronchoconstriction.

(3) The Oligo I attenuates bronchial hyperresponsiveness as measured by PC<sub>50</sub> histamine, a standard measurement to assess bronchial hyperresponsiveness. This result clearly demonstrates anti-inflammatory activity of the anti-sense oligo I as is shown in Table 5 above.

(4) As expected, because it was designed to target it, the anti-sense oligo I is totally specific for the adenosine A<sub>1</sub> receptor, and has no effect at all at any dose on either the very closely related adenosine A<sub>2</sub> receptor or the related bradykinin B<sub>2</sub> receptor. This is seen in Table 5 below.

(5) In contradistinction to the above effects of the Oligo I, the mismatch control molecules MM2 and MM3 (SEQ ID NO:11051 and SEQ ID NO:11052) which have identical base composition and molecular weight but differed from the anti-sense oligo I (SEQ ID NO: 9370) by 6 and 2 mismatches, respectively. These mismatches, which are the minimum possible while still retaining identical base composition, produced absolutely no effect upon any of the targeted receptors (A<sub>1</sub>, A<sub>2</sub> or B<sub>2</sub>).

These results, along with a complete lack of prior art on the use of anti-sense oligonucleotides, such as oligo I, targeted to the adenosine A<sub>1</sub> receptor, are unexpected results. The showings presented in this patent clearly enable and demonstrate the effectiveness, for their intended use, of the claimed agents and method for treating a disease or condition associated with lung airway, such as bronchoconstriction, inflammation, allergy(ies), and the like.

**Example 20: Oligo I Significantly Reduces  
Response to Adenosine Challenge**

The receptor binding experiment is described in Example 12 above, and the results shown in Table 5 below which shows the binding characteristics of the adenosine A<sub>1</sub>-selective ligand [<sup>3</sup>H]DPCPX and the bradykinin B<sub>2</sub>-selective ligand [<sup>3</sup>H]NPC 17731 in membranes isolated from airway smooth muscle of A<sub>1</sub> adenosine receptor and B<sub>2</sub> bradykinin receptor anti-sense- and mismatch-treated allergic rabbits.

**Table 5: Binding Characteristics of Three Anti-Sense Oligos**

Treatment <sup>1</sup>	A <sub>1</sub> receptor		B <sub>2</sub> receptor	
	K <sub>d</sub>	B <sub>max</sub>	K <sub>d</sub>	B <sub>max</sub>



Adenosine A <sub>1</sub>	Receptor			
20 mg	0.36±0.029 nM	19±1.52 fmoles*	0.39±0.031 nM	14.8±0.99fmoles
2 mg	0.38±0.030 nM	32±2.56 fmoles*	0.41±0.028 nM	15.5±1.08 fmoles
0.2 mg	0.37±0.030 nM	49±3.43 fmoles	0.34±0.024 nM	15.0±1.06 fmoles
<b>A<sub>1</sub>MM1</b>	<b>(Control)</b>			
20 mg	0.34±0.027 nM	52.0±3.64 fmoles	0.35±0.024 nM	14.0±1.0 fmoles
2 mg	0.37±0.033 nM	51.8±3.88 fmoles	0.38±0.028 nM	14.6±1.02 fmoles
<b>B<sub>2</sub>A (Bradykinin</b>	<b>Receptor)</b>			
20 mg	0.36±0.028 nM	45.0±3.15 fmoles	0.38±0.027 nM	8.7±0.62 fmoles*
2 mg	0.39±0.035 nM	44.3±2.90 fmoles	0.34±0.024 nM	11.9±0.76
0.2 mg	0.40±0.028 nM	47.0±3.76 fmoles	0.35±0.028 nM	15.1±1.05 fmoles
<b>B<sub>2</sub>MM (Control)</b>				
20 mg	0.39±0.031 nM	42.0±2.94 fmoles	0.41±0.029 nM	14.0±0.98 fmoles
2 mg	0.41±0.035 nM	40.0±3.20 fmoles	0.37±0.030 nM	14.8±0.99 fmoles
0.2 mg	0.37±0.029 nM	43.0±3.14 fmoles	0.36±0.025 nM	15.1±1.35 fmoles
Saline Control	0.37±0.041	46.0±5.21	0.39±0.047 nM	14.2±1.35 fmoles

**Example 21: Dose-response Effect of Oligo I**

Anti-sense oligo I (SEQ ID NO:9370) was found to reduce the effect of adenosine administration to the animal in a dose-dependent manner over the dose range tested as shown in Table 6 below.

**Table 6: Dose-Response Effect to Anti-sense Oligo I**

Total Dose (mg)	PC <sub>50</sub> Adenosine (mg Adenosine)
<b>Anti-sense Oligo I</b>	
0.2	8.32±7.2
2.0	14.0±7.2
20	19.5±0.34
<b>A<sub>1</sub>MM2 oligo (control)</b>	
0.2	2.51±0.46
2.0	3.13±0.71
20	3.25±0.34

The above results were studied with the Student's paired t test and found to be statistically different, p=0.05

The oligo I (SEQ ID NO:9370), an anti-adenosine A<sub>1</sub> receptor oligo, acts specifically on the adenosine A<sub>1</sub> receptor, but not on the adenosine A<sub>2</sub> receptors. These results stem from the treatment of rabbits with anti-sense oligo I (SEQ ID NO: 9370) or mismatch control oligo (SEQ ID NO:11051; A<sub>1</sub>MM2) as described in Example 9 above and in Nyce & Metzger (1997), supra (four doses of 5 mg spaced 8 to 12 hours apart via nebulizer via endotracheal tube), bronchial smooth muscle tissue excised and the number of adenosine A<sub>1</sub> and adenosine A<sub>2</sub> receptors determined as reported in Nyce & Metzger (1997), supra.

**Example 22: Specificity of Oligo I (SEQ ID NO:9370) for Target Gene Product**

Oligo I (SEQ ID NO:9370) is specific for the adenosine A<sub>1</sub> receptor whereas its mismatch controls had no activity. Figure 1 depicts the results obtained from the cross-over experiment described in Example 10 above and in Nyce & Metzger (1997), supra. The two mismatch controls (SEQ ID NO:11051 and SEQ ID NO:11052) evidenced no effect on the PC<sub>50</sub> Adenosine value. On the contrary, the administration of anti-sense oligo I (SEQ ID NO:9370) showed a seven-fold increase in the PC<sub>50</sub> Adenosine value. The results clearly indicate that the anti-sense oligo I (SEQ ID NO: 9370) reduces the response (attenuates the sensitivity) to exogenously administered adenosine

when compared with a saline control. The results provided in Table 6 above clearly establish that the effect of the anti-sense oligo I is dose dependent (see, column 3 of Table 5). The Oligo I was also shown to be totally specific for the adenosine A<sub>1</sub> receptor, (see, top 3 rows of Table), inducing no activity at either the closely related adenosine A<sub>2</sub> receptor or the bradykinin B<sub>2</sub> receptor (see, lines 8-10 of Table 6 above). In addition, the results shown in Table 6 establish that the anti-sense oligo I (SEQ ID NO:9370) decreases sensitivity to adenosine in a dose dependent manner, and that it does this in an anti-sense oligo-dependent manner since neither of two mismatch control oligonucleotides (A<sub>1</sub>MM2; SEQ ID NO:11051 and A<sub>1</sub>MM3; SEQ ID NO:11052) show any effect on PC<sub>50</sub> Adenosine values or on attenuating the number of adenosine A<sub>1</sub> receptors.

**Example 23: Effect on Aeroallergen-induced  
Bronchoconstriction & Inflammation**

The Oligo I (SEQ ID NO:9370) was shown to significantly reduce the histamine-induced effect in the rabbit model when compared to the mismatch oligos. The effect of the anti-sense Oligo I (SEQ ID NO:9370) and the mismatch oligos (A<sub>1</sub>MM2, SEQ ID NO:11051 and A<sub>1</sub>MM3, SEQ ID NO:11051) on allergen-induced airway obstruction and bronchial hyperresponsiveness was assessed in allergic rabbits. The effect of the anti-sense oligo I (SEQ ID NO:9370) on allergen-induced airway obstruction was assessed. As calculated from the area under the plotted curve, the anti-sense oligo I significantly inhibited allergen-induced airway obstruction when compared with the mismatched control (55%, p<0.05; repeated measures ANOVA, and Tukey's t test). A complete lack of effect was induced by the mismatch oligo A<sub>1</sub>MM2 (Control) on allergen induced airway obstruction. The effect of the anti-sense oligo I (SEQ ID NO:9370) on allergen-induced BHR was determined as above. As calculated from the PC<sub>50</sub> Histamine value, the anti-sense oligo I (SEQ ID NO:9370) significantly inhibited allergen-induced BHR in allergic rabbits when compared to the mismatched control (61%, p<0.05; repeated measures ANOVA, Tukey's t test). A complete lack of effect of the A<sub>1</sub>MM mismatch control on allergen-induced BHR was observed. The results indicated that anti-sense oligo I (SEQ ID NO: 9370) is effective to protect against aeroallergen-induced bronchoconstriction (house dust mite). In addition, the anti-sense oligo I (SEQ ID NO:9370) was also found to be a potent inhibitor of dust mite-induced bronchial hyper responsiveness, as shown by its effects upon histamine sensitivity which indicates anti-inflammatory activity for anti-sense oligo I (SEQ ID NO:1). The results indicated that anti-sense oligo I (SEQ ID NO 9370) is effective to protect against aeroallergen-induced bronchoconstriction (house dust mite). In addition, the anti-sense oligo I (SEQ ID NO: 9370) was also found to be a potent inhibitor of dust mite-induced bronchial hyper responsiveness, as shown by its effects upon histamine sensitivity which indicates anti-inflammatory activity for anti-sense oligo I (SEQ ID NO: 9370). The results indicated that anti-sense oligo I (SEQ ID NO: 9370) is effective to protect against aeroallergen-induced bronchoconstriction (house dust mite). In addition, the anti-sense oligo I (SEQ ID NO: 9370) was also found to be a potent inhibitor of dust mite-induced bronchial hyper responsiveness, as shown by its effects upon histamine sensitivity which indicates anti-inflammatory activity for anti-sense oligo I (SEQ ID NO: 9370). The results indicated that anti-sense oligo I (SEQ ID NO: 9370) is effective to protect against aeroallergen-induced bronchoconstriction (house dust mite). In addition, the anti-sense oligo I (SEQ ID NO: 9370) was also found to be a potent inhibitor of dust mite-induced bronchial hyper responsiveness, as shown by its effects upon histamine sensitivity which indicates anti-inflammatory activity for anti-sense oligo I (SEQ ID NO: 9370). The results indicated that anti-sense oligo I (SEQ ID NO: 9370) is effective to protect against aeroallergen-induced bronchoconstriction (house dust mite). In addition, the anti-sense oligo I (SEQ ID NO: 9370) was also found to be a potent inhibitor of dust mite-induced bronchial hyper responsiveness, as shown by its effects upon histamine sensitivity which indicates anti-inflammatory activity for anti-sense oligo I (SEQ ID NO: 9370).

**Example 24: Anti-sense Oligo I is Free  
of Deleterious Side Effects**

The Oligo I (SEQ ID NO: 9370) was shown to be free of side effects that might be toxic to the recipient. No changes in arterial blood pressure, cardiac output, stroke volume, heart rate, total peripheral resistance or heart

contractility (dPdT) were observed following administration of 2.0 or 20 mg oligo I (SEQ ID NO: 9370). The addition, the results of the measurement of cardiac output (CO), stroke volume (SV), mean arterial pressure (MAP), heart rate (HR), total peripheral resistance (TPR), and contractility (dPdT) with a CardiomaxJ apparatus (Columbus Instruments, Ohio) were assessed. These results evidenced that oligo I (SEQ ID NO: 9370) has no detrimental effect upon critical cardiovascular parameters. More particularly, this oligo does not cause hypotension. This finding is of particular importance because other phosphorothioate anti-sense oligonucleotides have been shown in the past to induce hypotension in some model systems. Furthermore, the adenosine A<sub>1</sub> receptor plays an important role in sinoatrial conduction within the heart. Attenuation of the adenosine A<sub>1</sub> receptor by anti-sense oligo I (SEQ ID NO: 9370) might be expected to result, therefore, in deleterious extrapulmonary activity in response to the downregulation of the receptor. This is not the case. The anti-sense oligo I (SEQ ID NO: 9370) does not produce any deleterious intrapulmonary effects and renders the administration of the low doses of the present anti-sense oligo free of unexpected, undesirable side effects. This demonstrates that when oligo I (SEQ ID NO: 9370) is administered directly to the lung, it does not reach the heart in significant quantities to cause deleterious effects. This is in contrast to traditional adenosine receptor antagonists like theophylline which do escape the lung and can cause deleterious, even life-threatening effects outside the lung.

**Example 25: Long Lasting Effect of Oligo I**

The Oligo I (SEQ ID NO: 9370) evidenced a long lasting effect as evidenced by the PC<sub>50</sub> and Resistance values obtained upon its administration prior to adenosine challenge. The duration of the effect was measured for with respect to the PC<sub>50</sub> of adenosine anti-sense oligo I when administered in four equal doses of 5 mg each by means of a nebulizer via an endotracheal tube, as described above. The effect of the agent is significant over days 1 to 8 after administration. When the effect of the anti-sense oligo I (SEQ ID NO: 9370) had disappeared, the animals were administered saline aerosols (controls), and the PC<sub>50</sub> Adenosine values for all animals were measured again. Saline-treated animals showed base line PC<sub>50</sub> adenosine values (n=6). The duration of the effect (with respect to Resistance) was measured for six allergic rabbits which were administered 20 mg of anti-sense oligo I (SEQ ID NO: 9370) as described above, upon airway resistance measured as also described above. The mean calculated duration of effect was 8.3 days for both PC<sub>50</sub> adenosine (p<0.05) and resistance (p<0.05). These results show that anti-sense oligo I (SEQ ID NO: 9370) has an extremely long duration of action, which is completely unexpected.

**Example 26: Anti-sense Oligo II**

Anti-sense oligo II, targeted to a different region of the adenosine A<sub>1</sub> receptor mRNA, was found to be highly active against the adenosine A<sub>1</sub>-mediated effects. The experiment measured the effect of the administration of anti-sense oligo II (SEQ ID NO: 9376) upon compliance and resistance values when 20 mg anti-sense oligo II or saline (control) were administered to two groups of allergic rabbits as described above. Compliance and resistance values were measured following an administration of adenosine or saline as described above in Example 13. The effect of the anti-sense oligo of the invention was different from the control in a statistically significant manner, p<0.05 using paired t-test, compliance; p<0.01 for resistance. The results showed that anti-sense oligo II (SEQ ID NO: 9376), which targets the adenosine A<sub>1</sub> receptor, effectively maintains compliance and reduces resistance upon adenosine challenge.

**Example 27: Antisense Oligos III and IV**

Oligos III (SEQ ID NO: 9377) and IV (SEQ ID NO: 9378) were shown to be in fact specifically targeted to the adenosine A<sub>3</sub> receptor by their effect on reducing inflammation and the number of inflammatory cells present upon separate administration of 20 mg of the anti-sense oligos III (SEQ ID NO: 9377) and IV (SEQ ID NO: 9378) to allergic rabbits as described above. The number of inflammatory cells was determined in their bronchial lavage fluid 3 hours later by counting at least 100 viable cells per lavage. The effect of anti-sense oligos III (SEQ ID NO: 9377) and IV (SEQ ID NO: 9378) upon granulocytes, and upon total cells in bronchial lavage were assessed following exposure to dust mite allergen. The results showed that the anti-sense oligo IV (SEQ ID NO: 9378) and anti-sense oligo III (SEQ ID NO: 9377) are very potent anti-inflammatory agents in the asthmatic lung following exposure to dust mite allergen. As is known in the art, granulocytes, especially eosinophils, are the primary inflammatory cells of asthma, and the administration of anti-sense oligos III (SEQ ID NO: 9377) and IV (SEQ ID NO: 9378) reduced their numbers by 40% and 66%, respectively. Furthermore, anti-sense oligos IV (SEQ ID NO: 9378) and III (SEQ ID NO: 9376) also reduced the total number of cells in the bronchial lavage fluid by 40% and

80%, respectively. This is also an important indicator of anti-inflammatory activity by the present anti-adenosine A<sub>3</sub> agents of the invention. Inflammation is known to underlie bronchial hyperresponsiveness and allergen-induced bronchoconstriction in asthma. Both anti-sense oligonucleotides III (SEQ ID NO: 9377) and IV (SEQ ID NO: 9378), which are targeted to the adenosine A<sub>3</sub> receptor, are representative of an important new class of anti-inflammatory agents which may be designed to specifically target the lung receptors of each species.

**Example 28: Anti-sense Oligo V**

The anti-sense oligo V (SEQ ID NO: 9379), targeted to the adenosine A<sub>2b</sub> adenosine receptor mRNA was shown to be highly effective at countering adenosine A<sub>2b</sub>-mediated effects and at reducing the number of adenosine A<sub>2b</sub> receptors present to less than half.

**Example 29: Unexpected Superiority of Substituted over Phosphodiester-residue Oligo I-DS (SEQ ID NO:1681)**

Oligos I (SEQ ID NO: 9370) and I-DS (SEQ ID NO: 11050) were separately administered to allergic rabbits as described above, and the rabbits were then challenged with adenosine. The phosphodiester oligo I-DS (SEQ ID NO: 11050) was statistically significantly less effective in countering the effect of adenosine whereas oligo I (SEQ ID NO: 9370) showed high effectiveness, evidencing a PC<sub>50 Adenosine</sub> of 20 mg.

**Example 30: Anti-sense Oligo VI**

For the present work, I designed an additional anti-sense phosphorothioate oligo targeted to the adenosine A<sub>1</sub> receptor (Oligo VI). This anti-sense oligo was designed for therapy on a selected species as described in the above patent application and is generally specific for that species, unless the segment of the adenosine receptor mRNA of other species elected happens to have a similar sequence. The anti-sense oligos were prepared as described below, and tested in vivo in a rabbit model for bronchoconstriction, inflammation and lung allergy, which have breathing difficulties and impeded lung airways, as is the case in ailments such as asthma, as described in the above-identified application. One additional oligo and its effect in a rabbit model was studied and the results of the study are reported and discussed below. The present oligo (anti-sense oligo VI) was selected for this study to complement the data on SEQ ID NO: 1 (Oligo I), which is anti-sense to the adenosine A<sub>1</sub> receptor mRNA provided in the above-identified patent application. This additional oligo is identified as anti-sense Oligo VI, and is targeted to a different region of the adenosine A<sub>1</sub> receptor mRNA than Oligo I. The design and synthesis of this anti-sense oligo was performed in accordance with the teaching, particularly Example 1, of the above-identified patent application. The anti-sense Oligo VI is a phosphorothioate designed to target the coding region of the rabbit adenosine A<sub>1</sub> receptor mRNA region +964 to +984 relative to the initiation codon (start site). The Oligo VI was prepared as described in the above-indicated application, and is 20 nucleotides long. The Oligo VI is directed to the adenosine A<sub>1</sub> receptor gene, and has the following sequence: 5'-CGC CGG CGG GTG CGG GCC GG-3' (SEQ ID NO: 12491). The phosphorothioate anti-sense Oligo VI having the sequence described in (5) above, was synthesized on an Applied Biosystems Model 396 Oligonucleotide Synthesizer, and purified using NENSORB chromatography (DuPont, DE). TETD (tetraethylthiuram disulfide) was used as the sulfurizing agent during the synthesis.

**Example 31: Preparation of Allergic Rabbits**

Neonatal New Zealand white Pasturella-free rabbits were immunized intraperitoneally within 24 hours of birth with 0.5 ml of 312 antigen units/ml house dust mite (*D. farinae*) extract (Berkeley Biologicals, Berkeley, CA) mixed with 10% kaolin as previously described (Metzger, W. J., in Late Phase Allergic Reactions, Dorsch, W., Ed., CRC Handbook, pp 347-362, CRC Press, Boca Raton, 1990; Ali, S. Et al., Am. J. Resp. Crit. Care Med. 149: 908 (1994)). The immunizations were repeated weekly for the first month and then bi-weekly until the animals were 4 months old. These rabbits preferentially produce allergen-specific IgE antibody, typically respond to aeroallergen challenge with both an early and late-phase asthmatic response, and show bronchial hyperresponsiveness (BHR). Monthly intraperitoneal administration of allergen (312 units dust mite allergen, as above) continues to stimulate and maintain allergen-specific IgE antibody and BHR. At 4 months of age, sensitized rabbits were prepared for aerosol administration as described by Ali et al. (1994), supra.

**Example 32: Adenosine Aerosol Preparation**

An adenosine aerosol (20 mg/ml) was prepared with an ultrasonic nebulizer (Model 646, DeVilbiss, Somerset, PA), which produced aerosol droplets, 80% of which were smaller than 5:μm in diameter. Equal volumes of the aerosols were administered directly to the lungs via an intratracheal tube to all three rabbits. The animals were then administered the aerosolized adenosine and Day 1 pre-treatment values for sensitivity to adenosine were calculated as the dose of adenosine causing a 50% loss of compliance (PC<sub>50</sub> Adenosine). The animals were then administered the aerosolized anti-sense via the intratracheal tube (5 mg/1.0 ml), for 2 minutes, twice daily for 2 days (total dose, 20 mg). Post-treatment PC<sub>50</sub> values were recorded (post-treatment challenge) on the morning of the third day. The results of these studies are provided in (9) below.

**Example 33: Anti-sense Oligo Formulation**

Each one of anti-sense oligos were separately solubilized in an aqueous solution and administered as described for anti-sense oligo I in (c) above, in four 5 mg aliquots (20 mg total dose) by means of a nebulizer via endotracheal tube, as described above.

**Example 34: Oligo VI Reduces Response to Adenosine Challenge as well or Better than Oligo I**

Oligo VI was tested in three allergic rabbits of the characteristics and readied as described in (7) above and in the above-indicated patent application. Oligo VI targets a section of the coding region of the A<sub>1</sub> receptor which is different from Oligo I. Both these target sequences were selected randomly from many possible coding region target sequences. The three rabbits were treated identically as previously indicated for Oligo I. Briefly, 5 mg of Oligo VI were nebulized to the rabbits twice per day at 8 hour intervals, for two days. Thereafter, PC<sub>50</sub> adenosine studies were performed on the morning of the third day and compared to pre-treatment PC<sub>50</sub> values. This protocol is described in more detail in Nyce and Metzger (Nyce & Metzger, Nature 385: 721-725 (1997)). The results obtained for the three rabbits are shown in Table 7 below.

**Table 7: PC<sub>50</sub> Adenosine before & after Aerosolized Adenosine Treatment**

Treatment Time	PC <sub>50</sub> Adenosine (mg)
Pre-treatment	3.0 ±2.1
Post-treatment	>20.0*

\* maximum achievable dose due to adenosine insolubility in saline

All three animals treated with Oligo VI completely eliminated sensitivity to adenosine up to the measurable level of the agent shown in Table 7 above. That is, the administration of the Oligo VI abrogated the adenosine-induced bronchoconstriction in the three allergic rabbits. The actual efficacy of Oligo VI is, therefore, greater than could be measured in the experimental system used. By comparing with the previously submitted results for the Oligo I, it may be seen that the Oligo VI was found to be as effective, or more, than Oligo I.

**Example 34: Conclusions**

The work described and results discussed in the examples clearly indicates that all anti-sense oligonucleotides designed in accordance with the teachings of the above-identified application were found to be highly effective at countering or reducing effects mediated by the receptors they are targeted to. That is, each and all of the two anti-sense oligos targeting an adenosine A<sub>1</sub> receptor mRNA, 1 anti-sense oligo targeting an adenosine A<sub>2b</sub> receptor mRNA, and the 2 anti-sense oligos targeting an A<sub>3</sub> receptor mRNA were shown capable of countering the effect of exogenously administered adenosine which is mediated by the specific receptor they are targeted to. The activity of the anti-sense oligos of this invention, moreover, is specific to the target and substitutively fails to inhibit another target. In addition, the results presented also show that the administration of the present agents results in extremely low or non-existent deleterious side effects or toxicity. This represents 100% success in providing agents that are highly effective and specific in the treatment of bronchoconstriction and/or inflammation. This invention is broadly applicable in the same manner to all gene(s) and corresponding mRNAs encoding proteins involved in or associated with airway diseases. A comparison of the phosphodiester and a version of the same oligonucleotide wherein the phosphodiester bonds are substituted with phosphorothioate bonds evidenced an unexpected superiority for the phosphothiorate oligonucleotide over the phosphodiester anti-sense oligo.

**Example 35: In Vivo Response to Adenosine Challenge**

#### with & without Oligo I Pretreatment

Two hyper responsive monkeys (ascaris sensitive) were challenged with inhaled adenosine, with and without pre-treatment with anti-sense oligo I (SEQ ID NO: 9370). The PC<sub>40</sub> adenosine was calculated from the data collected as being equivalent to that amount of adenosine in mg that causes a 40% decrease in dynamic compliance in hyper-responsive airways. The Oligo I (SEQ ID NO: 9370; EPI 2010) was subsequently administered at 10 mg/day for 2 days by inhalation. On the third day, the PC adenosine was again measured. The PC<sub>40</sub> adenosine value prior to treatment with Oligo I was compared side-by-side with to the PC<sub>40</sub> adenosine taken after administration of Oligo I (Figure not shown). The results of the experiment conducted with two animals showed that any sensitivity to adenosine was completely eliminated by the administration of the oligo of this invention in one animal, and substantially reduced in the second.

#### **Example 36: Extension of the experimental Results**

The method of the present invention is also practiced with anti-sense oligonucleotides targeted to many genes, mRNAs and their corresponding proteins as described above, in essentially the same manner as given above, for the treatment of various conditions in the lungs. Examples of these are Human A<sub>2a</sub> adenosine receptor, Human A<sub>2b</sub> adenosine receptor, Human IgE receptor  $\beta$ , Human Fc-epsilon receptor CD23 antigen (IgE receptor), Human IgE receptor,  $\alpha$  subunit, Human IgE receptor, Fc epsilon R, Human histidine decarboxylase, Human beta tryptase, Human tryptase-I, Human prostaglandin D synthase, Human cyclooxygenase-2, Human eosinophil cationic protein, Human eosinophil derived neurotoxin, Human eosinophil peroxidase, Human intercellular adhesion molecule-1 (ICAM-1), Human vascular cell adhesion molecule 1 (VCAM-1), Human endothelial leukocyte adhesion molecule (ELAM-1), Human P Selectin, Human endothelial monocyte activating factor, Human IL3, Human IL4, Human IL5, Human IL6, Human monocyte-derived neutrophil chemotactic factor, Human neutrophil elastase (medullasin), Human neutrophil oxidase factor, Human cathepsin G, Human defensin 1, Human defensin 3, Human macrophage inflammatory protein-1-alpha, Human muscarinic acetylcholine receptor HM1, Human muscarinic acetylcholine receptor HM3, Human fibronectin, Human interleukin 8, Human GM-CSF, Human tumor necrosis factor  $\alpha$ , Human leukotriene C4 synthase, Human major basic protein, and many more.

#### **Example 37: In Vivo Effects of Folinic Acid and DHEA on Adenosine Levels**

In the examples provided below, EA means an epiandrosterone, DHEA means dehydroepiandrosterone, s means seconds, mg means milligrams, kg means kilograms, kw means kilowatts, Mhz means megahertz, CoQ means a ubiquinone, and nmol means nanomoles.

Young adult male Fischer 344 rats (120 grams) were administered dehydroepiandrosterone (DHEA) (300 mg/kg) or methyltestosterone (40 mg/kg) in carboxymethylcellulose by gavage once daily for fourteen days. Folinic acid (50 mg/kg) was administered intraperitoneally once daily for fourteen days. On the fifteenth day, the animals were sacrificed by microwave pulse (1.33 kw, 2450 MHZ, 6.5 s) to the cranium, which instantly denatures all brain protein and prevents further metabolism of adenosine. Hearts were removed from animals and flash frozen in liquid nitrogen with 10 seconds of death. Liver and lungs were removed en bloc and flash frozen with 30 seconds of death. Brain tissue was subsequently dissected. Tissue adenosine was extracted, derivatized to 1, N6-ethenoadenosine and analyzed by high performance liquid chromatography (HPLC) using spectrofluorometric detection according to the method of Clark and Dar (J. of Neuroscience Methods 25:243 (1988)). Results of these experiments are summarized in Table 1 below. Results are expressed as the mean  $\pm$  SEM, with ?  $p < 0.05$  compared to control group and  $\psi$   $p < 0.05$  compared to DHEA or methyltestosterone-treated groups.

**Table 1: In Vivo Effect of DHEA,  $\delta$ -1-methyltestosterone & Folinic Acid on Adenosine Levels in Various Rat Tissues**

	Intracellular Adenosine (nmol/mg protein)		
	Heart	Lung	Brain
Control	10.6 $\pm$ 0.6 (n=12)	3.1 $\pm$ 0. (n=6)	0.5 $\pm$ 0.04 (n=12)
DHEA (300 mg/kg)	6.7 $\pm$ 0.5 (n=12)	2.3 $\pm$ 0.3 (n=6)	0.19 $\pm$ 0.01 (n=12)
Methyltestosterone (40 mg/kg)	8.3 $\pm$ 1.0 (n=6)	N.D.	0.42 $\pm$ 0.06 (n=6)
Methyltestost. (M) (120mg/kg)	6.0 $\pm$ 0.4 (n=6)	N.D.	0.32 $\pm$ 0.03 (n=6)
Folinic Acid (F.A.) (50mg/kg)	12.4 $\pm$ 2.1 (n=5)	N.D.	0.72 $\pm$ 0.09 (n=5)
DHEA+ F.A. (300mg/kg;50mg/kg)	11.1 $\pm$ 0.6 (n=5)	N.D.	0.55 $\pm$ 0.09 (n=5)
M + F.A. (120mg/kg;50mg/kg)	9.1 $\pm$ 0.4 (n=6)	N.D.	0.60 $\pm$ 0.06 (n=6)
N.D. = Not Determined			

The results of these experiments indicate that rats administered DHEA or methyltestosterone daily for two weeks showed multi-organ depletion of adenosine. Depletion was dramatic in brain (60% depletion for DHEA, 34% for high dose methyltestosterone) and heart (37% depletion for DHEA, 22% depletion for high dose methyltestosterone). Co-administration of folinic acid completely abrogated steroid-mediated adenosine depletion. Folinic acid administered alone induce increase in adenosine levels for all organs studied.

**Example 38: Preparation of the Experimental Model**

Cell cultures, HT-29 SF cells, which represent a subline of HY-29 cells (ATCC, Rockville, Md.) and are adapted for growth in completely defined serum-free PC-1 medium (Ventrex, Portland, Me.), were obtained. Stock cultures were maintained in this medium at 37° in a humidified atmosphere containing 5% CO<sub>2</sub>. At confluence cultures were replated after dissociation using trypsin/EDTA (Gibco, Grand Island, N.Y.) and re-fed every 24 hours. Under these conditions, the doubling time for HT-29 SF cells during logarithmic growth was 24 hours.

**Example 39: Flow Cytometry**

Cells were plated at 10<sup>5</sup>/60-mm dish in duplicate. For analysis of cell cycle distribution, cultures were exposed to either 0, 25, 50, or 200  $\mu$ M DHEA. For analysis of reversal of cell cycle effects of DHEA, cultures were exposed to either 0 or 25  $\mu$ M DHEA, and the media were supplemented with MVA, CH, RN, MVA plus CH, or MVA plus CH plus RN or were not supplemented. Cultures were trypsinized following 0, 24, 48, or 74 hours and fixed and stained using a modification of a procedure of Bauer et al., *Cancer Res.*, 46, 3173-3178 (1986). Briefly, cells were collected by centrifugation and resuspended in cold phosphate-buffered saline. Cells were fixed in 70% ethanol, washed, and resuspended in phosphate-buffered saline. One ml hypotonic stain solution [50  $\mu$ g/ml propidium iodide (Sigma Chemical Co.), 20  $\mu$ g/ml Rnase A (Boehringer Mannheim, Indianapolis, Ind.), 30 mg/ml polyethylene glycol, 0.1% Triton X-100 in 5 mM citrate buffer] was then added, and after 10 min at room temperature, 1 ml of isotonic stain solution [propidium iodide, polyethylene glycol, Triton X-100 in 0.4M NaCl] was added and the cells were analyzed using a flow cytometer, equipped with pulse width/pulse area doublet discrimination (Becton Dickinson Immunocytometry Systems, San Jose, Calif.) After calibration with fluorescent beads, a minimum of 2x10<sup>4</sup> cells/sample were analyzed, data were displayed as total number of cells in each of 1024 channels of increasing fluorescence intensity, and the resulting histogram was analyzed using the Cellfit analysis program (Becton Dickinson).

**Example 40: DHEA Effect on Cell Growth**

Cells were plated 25,000 cells/30 mm dish in quadruplicate, and after 2 days received 0, 12.5, 25, 50, or 200  $\mu$ M DHEA. Cell number was determined 0, 24, 48, and 72 hours later using a Coulter counter (model Z, Coulter Electronics, Inc. Hialeah, Fla.). DHEA (AKZO, Basel, Switzerland) was dissolved in dimethyl sulfoxide,



filter sterilized, and stored at -20°C until use.

Figure 1 illustrates the inhibition of growth for HT-29 cells by DHEA. Points refer to numbers of cells, and bars refer to SEM. Each data point was performed in quadruplicate, and the experiment was repeated three times. Where SEM bars are not apparent, SEM was smaller than symbol. Exposure to DHEA resulted in a reduced cell number compared to controls after 72 hours in 12.5  $\mu$ M, 48 hours in 25 or 50  $\mu$ M, and 24 hours in 200  $\mu$ M DHEA, indicating that DHEA produced a time- and dose-dependent inhibition of growth.

**Example 41: DHEA Effect on Cell Cycle**

To examine the effects of DHEA on cell cycle distribution, HT-29 SF cells were plated ( $10^5$  cells/60 mm dish), and 48 hours later treated with 0, 25, 50, or 200  $\mu$ M DHEA. FIG. 2 illustrates the effects of DHEA on cell cycle distribution in HT-29 SF cells. After 24, 48, and 72 hours, cells were harvested, fixed in ethanol, and stained with propidium iodide, and the DNA content/cell was determined by flow cytometric analysis. The percentage of cells in G<sub>1</sub>, S, and G<sub>2</sub>M phases was calculated using the Cellfit cell cycle analysis program. S phase is marked by a quadrangle for clarity. Representative histograms from duplicate determinations are shown. The experiment was repeated three times.

The cell cycle distribution in cultures treated with 25 or 50  $\mu$ M DHEA was unchanged after the initial 24 hours. However, as the time of exposure to DHEA increased, the proportion of cells in S phase progressively decreased, and the percentage of cells in G<sub>1</sub>, S and G<sub>2</sub>M phases was calculated using the Cellfit cell cycle analysis program. S phase is marked by a quadrangle for clarity. Representative histograms from duplicate determinations are shown. The experiment was repeated three times.

The cell cycle distribution in cultures treated with 25 or 50  $\mu$ M DHEA was unchanged after the initial 24 hours. However, as the time of exposure to DHEA increased, the proportion of cells in S phase progressively decreased and the percentage of cells in G<sub>1</sub> phase was increased after 72 hours. A transient increase in G<sub>2</sub>M phase cells was apparent after 48 hours. Exposure to 200  $\mu$ M DHEA produced a similar but more rapid increase in the percentage of cells in G<sub>1</sub> and a decreased proportion of cells in S phase after 24 hours, which continued through the treatment. This indicates that DHEA produced a G<sub>1</sub> block in HT-29 SF cells in a time- and dose-dependent manner.

**Example 42: Reversal of DHEA-mediated Effect on Growth & Cell Cycle**

Reversal of DHEA-mediated Growth Inhibition. Cells were plated as above, and after 2 days received either 0 or 25  $\mu$ M DHEA-containing medium supplemented with mevalonic acid ("MVA"; 2 mM) squalene ("SQ"; 80  $\mu$ M), cholesterol ("CH"; 15  $\mu$ g/ml), MVA plus CH, ribonucleosides ("RN"; uridine, cytidine, adenosine, and guanosine at final concentrations of 30  $\mu$ M each), deoxyribonucleosides ("DN"; thymidine, deoxycytidine, deoxyadenosine and deoxyguanosine at final concentrations of 20  $\mu$ M each). RN plus DN, or MVA plus CH plus RN, or medium that was not supplemented. All compounds were obtained from Sigma Chemical Co. (St. Louis, Mo.) Cholesterol was solubilized in ethanol immediately before use. RN and DN were used in maximal concentrations shown to have no effects on growth in the absence of DHEA.

Figure 3 illustrates the reversal of DHEA-induced growth inhibition in HT-29 SF cells. In A, the medium was supplemented with 2  $\mu$ M MVA, 80  $\mu$ M SQ, 15  $\mu$ g/ml CH, or MVA plus CH (MVA+CH) or was not supplemented (CON). In B, the medium was supplemented with a mixture of RN containing uridine, cytidine, adenosine, and guanosine in final concentrations of 30  $\mu$ M each; a mixture of DN containing thymidine, deoxycytidine, deoxyadenosine and deoxyguanosine in final concentrations of 20  $\mu$ M each; RN plus DN (RN+DN); or MVA plus CH plus RN (MVA+CH+RN). Cell numbers were assessed before and after 48 hours of treatment, and culture growth was calculated as the increase in cell number during the 48 hour treatment period. Columns represent cell growth percentage of untreated controls; bars represent SEM. Increase in cell number in untreated controls was  $173,370 \pm 6518$ . Each data point represents quadruplicate dishes from four independent experiments. Statistical analysis was performed using Student's t test;  $\psi$   $p < 0.01$ ;  $\kappa$   $p < 0.001$ ; compared to treated controls. Note that supplements had little effect on culture growth in absence of DHEA.

Under these conditions, the DHEA-induced growth inhibition was partially overcome by addition of MVA as well as by addition of MVA plus CH. Addition of SQ or CH alone had no such effect. This suggests that the cytostatic activity of DHEA was in part mediated by depletion of endogenous mevalonate and subsequent inhibition of the biosynthesis of an early intermediate in the cholesterol pathway that is essential for cell growth. Furthermore, partial reconstitution of growth was found after addition of RN as well as after addition of RN plus DN but not after addition of DN, indicating that depletion of both mevalonate and nucleotide pools is involved in the growth-inhibitory action of DHEA. However, none of the reconstitution conditions including the combined addition of

MVA, CH, and RN completely overcame the inhibitory action of DHEA, suggesting either cytotoxic effects or possibly that additional biochemical pathways are involved.

**Example 43: Reversal of DHEA Effect on Cell Cycle**

HT-29 SF cells were treated with 25 FM DHEA in combination with a number of compounds, including MVA, CH, or RN, to test their ability to prevent the cell cycle-specific effects of DHEA. Cell cycle distribution was determined after 48 and 72 hours using flow cytometry.

Figure 4 illustrates reversal of DHEA-induced arrest in HT-29 SF cells. Cells were plated ( $10^5$  cells/60 mm dish) and 48 hours later treated with either 0 or 25 FM DHEA. The medium was supplemented with 2 FM MVA; 15 Fg/ml CH; a mixture of RN containing uridine, cytidine, adenosine, and guanosine in final concentrations of 30 FM; MVA plus CH (MVA+CH); or MVA plus CH plus RN (MVA+CH+RN) or was not supplemented. Cells were harvested after 48 or 72 hours, fixed in ethanol, and stained with propidium iodide, and the DNA content per cell was determined by flow cytometric analysis. The percentage of cells in G<sub>1</sub>, S, and G<sub>2</sub>M phases were calculated using the Cellfit cell cycle profile analysis program. S phase is marked by a quadrangle for clarity. Representative histograms from duplicative determinations are shown. The experiment was repeated two times. Note that supplements had little effect on cell cycle progression in the absence of DHEA.

With increasing exposure time, DHEA progressively reduced the proportion of cells in S phase. While inclusion of MVA partially prevented this effect in the initial 48 hours but not after 72 hours, the addition of MVA plus CH was also able to partially prevent S phase depletion at 72 hours, suggesting a requirement of both MVA and CH for cell progression during prolonged exposure. The addition of MVA, CH, and RN was apparently most effective at reconstitution but still did not restore the percentage of S phase cells to the value seen in untreated control cultures. CH or RN alone had very little effect at 48 hours and no effect at 72 hours. Morphologically, cells responded to DHEA by acquiring a rounded shape, which was prevented only by the addition of MVA to the culture medium (data not shown). Some of the DNA histograms after 72 hours DHEA exposure in FIG.4 also show the presence of a subpopulation of cells possessing apparently reduced DNA content. Since the HT-29 cell line is known to carry populations of cells containing varying numbers of chromosomes (68-72; ATCC), this may represent a subset of cells that have segregated carrying fewer chromosomes.

**Example 44: Conclusions**

The examples above provide evidence that in vitro exposure of HT-29 SF human colonic adenocarcinoma cells to concentrations of DHEA known to deplete endogenous mevalonate results in growth inhibition and G<sub>1</sub> arrest and that addition of MVA to the culture medium in part prevents these effects. DHEA produced effects upon protein isoprenylation which were in many respects similar to those observed for specific 3-hydroxy-3-methylglutaryl-CoA reductase inhibitors such as lovastatin and compactin. Unlike direct inhibitors of mevalonate biosynthesis, however, DHEA mediates its effects upon cell cycle progression and cell growth in a pleiotropic manner involving ribo- and deoxyribonucleotide biosynthesis and possibly other factors as well.

The foregoing examples are illustrative of the present invention, but should not to be construed as limiting thereof. The invention is defined by the following claims, with equivalents of the claims to be included therein.

**Example 45: Effect of CoQs & an EA on In Vitro NADPH Levels**

Glucose-6-Phosphate Dehydrogenase (G6PD) is an important enzyme that is widespread in mammals, and is involved in the conversion of NADP to NADPH, thereby increasing NADPH levels. An inhibition of the G6PD enzyme, thus, will be expected to result in a reduction of cellular NADPH levels, which event, in turn, will be expected to inhibit pathways that are heavily dependent on NADPH. One such pathway, the so-called One-Carbon-Pool pathway, also known as the Folate Pathway, is directly involved in the production of adenosine by addition of the C<sub>2</sub> and C<sub>8</sub> carbon atoms of the purine ring. Consequently, the inhibition of this pathway will lead to adenosine depletion.

The present invention is broadly applicable to dehydroepiandrosterones (DHEAs) and Ubiquinones (CoQs). The description of the pathways involved in the present invention are described in the Background section. The present experiment was designed to show that one DHEA and two CoQs inhibit NADPH levels. DHEA, an dehydroepiandrosterone, has already been shown to decrease levels of adenosine in various tissues. See, Examples 1 and 2 above. The fact that two CoQs are shown to lower NADPH levels to a similar extent as a dehydroepiandrosterone, let alone to a similar extent ensures that the NADPH reduction caused by the CoQs will

also result in lower cellular adenosine levels or in adenosine cell depletion. Thus, in accordance with the invention, both dehydroepiandrosterones and Ubiquinones decrease levels of adenosine and, therefore, are useful as medicaments for use in the treatment of diseases where a decrease of adenosine levels or its depletion is desirable, including respiratory diseases such as asthma, bronchoconstriction, lung inflammation and allergies and the like.

Both Ubiquinones and DHEA inhibit NADPH levels in a statistically significant manner, when compared to a control. Moreover, the Ubiquinone inhibits NADPH levels to a similar extent as DHEA. The present invention is broadly applicable to the use of dehydroepiandrosterones (DHEAs) and Ubiquinones (CoQs) to the treatment of respiratory and lung diseases, and other diseases associated with varying levels of adenosine, adenosine hypersensitivity, asthma, bronchoconstriction, and/or lung inflammation and allergies. The DHEA and Ubiquinones employed in the present experiments are equivalent to those described and exemplified above.

#### Enzymatic assay of purified G6PDH

The reaction mixture contained 50mM glycyl glycine buffer, pH 7.4, 2 mM D-glucose-6-phosphate, 0.67 mM Beta-NADP, 10 mM MgCL<sub>2</sub> and 0.0125 units of G6PDH in a final volume of 3.0 ml. All experiments were repeated 4 times.

The control group contained 3 samples that were added no DHEA or ubiquinone. The experimental group contained a similar number of samples (3) for each concentration of DHEA or ubiquinone. One group was added DHEA (in triplicate) at different concentrations. A second group was added different concentrations of a CoQ of long side chain (in triplicate), and a third group received a CoQ of short side chain (in triplicate), both at various doses in the  $\mu$ M range.

The reaction was started by addition of the enzyme, and the increase in absorbance at 340 nm was measured for 5 minutes. Each data point was conducted in triplicate, and the full experiment was repeated 4 times.

Both DHEA and the ubiquinones inhibited the enzyme activity in a statistically significant manner when compared to controls. DHEA was found to inhibit by 72% in vitro the activity of purified G6PDH when compared to control. Both ubiquinones inhibited the activity of purified G6PDH in vitro by an amount that was not statistically significantly different from that of DHEA. Both DHEA and the ubiquinones inhibited the enzyme in a statistically significant manner when compared to controls. Both long chain and short chain CoQs were found to be effective inhibitors of G6PDH.

The above results clearly indicate that CoQ reduced cellular levels of NADPH to an extent similar to DHEA and consequently cellular adenosine levels, and has a therapeutic effect on diseases and conditions associated with them. The present results show that CoQs have a therapeutic effect similar to that of dehydroepiandrosterones. The pathways involved in the present invention, as described above, show the criticality of the results reported here, showing that a dehydroepiandrosterone (DHEA) and two ubiquinones inhibit NADPH levels in a statistically significant manner. The same dehydroepiandrosterone (DHEA) was shown in Examples 1 and 2 to decrease levels of adenosine in various tissues. The two different ubiquinones employed lowered NADPH levels to a similar extent as DHEA. The NADPH reduction caused by the ubiquinones will, in the case of DHEA, result in lower cellular adenosine levels or adenosine depletion. Thus, in accordance with the invention, both dehydroepiandrosterones and ubiquinones decrease levels of adenosine and are, therefore, useful in the therapy of diseases and conditions where a decrease of adenosine levels or its depletion are desirable, including respiratory and airway diseases such as asthma, bronchoconstriction, lung inflammation and allergies, and the like.

In Examples 46 to 51, micronized anti-sense oligo targeting the adenosine A<sub>1</sub> receptor (EPI 2010) and micronized salmeterol (as the hydroxynaphthoate) are added in the proportions given below either dry or after predispersal in a small quantity of stabilizer, disodium dioctylsulphosuccinate, lecithin, oleic acid or sorbitan solvent to a suspension vessel containing the main bulk of the solvent. The resulting suspension is further dispersed by an appropriate mixing system using, for example, a high shear blender, ultrasonics or a microfluidiser until an ultrafine dispersion is created. The suspension is then continuously recirculated to suitable filling equipment designed for cold fill or pressure filling of solvent. The suspension may be also prepared in a suitable chilled solution of stabilizer, in solvent.

#### Example 46: Metered Dose Inhaler

Active Ingredient	Target per Actuation
DHEA	200 mg

EPI 2010	1 mg
Stabilizer	5.0 µg
Solvent (1)	23.70 mg
Solvent (2)	61.25 mg

**Example 47: Metered Dose Inhaler**

Active Ingredient	Target per Actuation
DHEA-S	200 mg
EPI 2010	5 mg
Stabilizer	7.5 µg
Solvent (1)	23.67 mg
Solvent (2)	61.25 mg

**Example 48: Metered Dose Inhaler**

Active Ingredient	Target per Actuation
Ubiquinone (CoQ10)	200 mg
EPI 2010	30 mg
Stabilizer	25.0 µg
Solvent (1)	23.45 mg
Solvent (2)	61.25 mg

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**Example 49: Metered Dose Inhaler**

Active Ingredient	Target per Actuation
DHEA	600 mg µg
EPI 2010	1.0 mg
Stabilizer	15.0 µg
Solvent (1)	23.56 mg
Solvent (2)	61.25 mg

**Example 50: Metered Dose Inhaler**

Active Ingredient	Target per Actuation
DHEA-S	600 mg
EPI 2010	5.0 mg
Stabilizer	15.0 µg
Solvent (1)	23.56 mg
Solvent (2)	61.25 mg

10 **Example 51: Metered Dose Inhaler**

Active Ingredient	Target per Actuation
Ubiquinone	600 mg
EPI 2010	30.0 mg
Stabilizer	25.0 µg
Solvent (1)	23.43 mg
Solvent (2)	61.25 mg

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In the following Examples 43 to 48, the active ingredients are micronized and bulk blended with lactose in the proportions given above. The blend is filled into hard gelatin capsules or cartridges or into specifically constructed double foil blister packs (Rotadisks blister packs, Glaxo® to be administered by an inhaler such as the Rotahaler inhaler (Glaxo®) or in the case of the blister packs with the Diskhaler inhaler (Glaxo®).

**Example 52: Metered Dose Dry Powder Formulation**

Active Ingredient	/cartridge or blister
DHEA	1 mg
EPI 2010	0.05 mg
Lactose Ph. Eur.	to 12.5 or 25.0 mg

**Example 53: Metered Dose Dry Powder Formulation**

Active Ingredient	/cartridge or blister
DHEA-S	1 mg
EPI 2010	0.1 mg
Lactose Ph. Eur.	to 12.5 or 25.0 mg

**Example 54: Metered Dose Dry Powder Formulation**

Active Ingredient	/cartridge or blister
Ubiquinone	1 mg
EPI 2010	0.15 mg
Lactose Ph. Eur.	to 12.5 or 25.0 mg

**Example 55: Metered Dose Dry Powder Formulation**

Active Ingredient	/cartridge or blister
DHEA	1 mg
EPI 2010	0.01 mg
Lactose Ph. Eur.	to 12.5 or 25.0 mg

**Example 56: Metered Dose Dry Powder Formulation**

Active Ingredient	/cartridge or blister
DHEA-S	1 mg
EPI 2010	0.05 mg
Lactose Ph. Eur.	to 12.5 or 25.0 mg

**Example 57: Metered Dose Dry Powder Formulation**

Active Ingredient	/cartridge or blister
Ubiquinone	1 mg
EPI 2010	0.1 mg
Lactose Ph. Eur.	to 12.5 or 25.0 mg

**Example 58: Metered Dose Inhaler Formulation (1)**

Standard 12.5 ml MDI (metered dose inhaler) cans (Presspart Inc., Cary N.C.) are spray-coated with PTFE-FEP-polyamideimide blend (DuPont) and cured according to the vendor's standard procedure. The thickness of the coating is between approximately 1  $\mu$ m and approximately 20  $\mu$ m. These cans are then purged of air the valves crimped in place, and a suspension of about 68 mg of micronised beclomethasone dipropionate monohydrate and 1 mg of oligonucleotide in about 6.1 mg water and about 18.2 g P134a is filled through the valve.

**Example 59: Metered Dose Inhaler Formulation (2)**

Standard 12.5 ml MDI cans (Presspart Inc., Cary N.C.) are spray-coated with PTFE-FEP-polyamideimide blend (DuPont) and cured according to the vendor's standard procedure. The thickness of the coating is between approximately 1  $\mu$ m and approximately 20  $\mu$ m. These cans are then purged of air the valves crimped in place, and about 50 mg of dehydroepiandrosterone, 1 mg of micronised oligonucleotide and 50 mg of Coenzyme Q10 in about 182 mg ethanol and about 18.2 g P134a is filled through the valve.

**Example 60: Metered Dose Inhaler Formulation (3)**

Standard 12.5 ml MDI cans (Presspart Inc., Cary N.C.) are spray-coated with PTFE-PES blend (DuPont) as a single coat and cured according to the vendor's standard procedure. The thickness of the coating is between approximately 1  $\mu\text{m}$  and approximately 20  $\mu\text{m}$ . These cans are then purged of air, the valves crimped in place, and a suspension of about 41.0 mg, 21.0 mg, 8.8 mg or 4.4 mg of micronised fluticasone propionate and 2 mg of micronised oligonucleotide in about 12 g P134a is filled through the valve.

**Example 61: Metered Dose Inhaler Formulation (4)**

Standard 12.5 ml MDI cans (Presspart Inc., Cary N.C.) are spray-coated with PTFE-PES blend (DuPont) as a single coat and cured according to the vendor's standard procedure. The thickness of the coating is between approximately 1  $\mu\text{m}$  and approximately 20  $\mu\text{m}$ . These cans are then purged of air, the valves crimped in place, and a suspension of about 8.8 mg, 22 mg or 44 mg of micronised fluticasone propionate with about 6.4 mg of micronised salmeterol xinafoate and 1 mg of micronised oligonucleotide in about 12 g P134a is filled through the valve.

**Example 62: Metered Dose Inhaler Formulation (5)**

Standard 12.5 ml MDI cans (Presspart Inc., Cary N.C.) are spray-coated with PTFE-FEP-polyamideimide blend (DuPont) and cured according to the vendor's standard procedure. The thickness of the coating is between approximately 1  $\mu\text{m}$  and approximately 20  $\mu\text{m}$ . These cans are then purged of air the valves crimped in place, and a suspension of about 50mg of micronised dehydroepiandrosterone with about 6.4 mg of micronised salmeterol xinafoate and 2 mg of micronised oligonucleotide in about 12 g P134a is filled through the valve.

**Example 63: Metered Dose Inhaler Formulation (6)**

Standard 12.5 ml MDI cans (Presspart Inc., Cary N.C.) are spray-coated with PTFE-PES blend (DuPont) as a single coat and cured according to the vendor's standard procedure. The thickness of the coating is between approximately 1  $\mu\text{m}$  and approximately 20  $\mu\text{m}$ . These cans are then purged of air, the valves crimped in place, and a suspension of about 50 mg of micronised dehydroepiandrosterone sulfate and 2 mg of micronised oligonucleotide in about 12 g P134a is filled through the valve.

**Example 64: Effect of CoQs & an EA on In Vitro NADPH Levels**

Glocose-6-Phosphate Dehydrogenase (G6PD) is an important enzyme that is widespread in mammals, and is involved in the conversion of NADP to NADPH, thereby increasing NADPH levels. An inhibition of the G6PD enzyme, thus, will be expected to result in a reduction of cellular NADPH levels, which event, in turn, will be expected to inhibit pathways that are heavily dependent on NADPH. One such pathway, the so-called One-Carbon-Pool pathway, also known as the Folate Pathway, is directly involved in the production of adenosine by addition of the C<sub>2</sub> and C<sub>8</sub> carbon atoms of the purine ring. Consequently, the inhibition of this pathway will lead to adenosine depletion.

The present invention is broadly applicable to Epiandrosterones (EAs) and Ubiquinones (CoQs). The description of the pathways involved in the present invention are described in the Background section. The present experiment was designed to show that one EA and two CoQs inhibit NADPH levels. DHEA, an Epiandrosterone, has already been shown to decrease levels of adenosine in various tissues. See, Examples 1 and 2 above. The fact that two CoQs are shown to lower NADPH levels to a similar extent as an Epiandrosterone, let alone to a similar extent ensures that the NADPH reduction caused by the CoQs will also result in lower cellular adenosine levels or in adenosine cell depletion. Thus, in accordance with the invention, both Epiandrosterones and Ubiquinones decrease levels of adenosine and, therefore, are useful as medicaments for use in the treatment of diseases where a decrease of adenosine levels or its depletion is desirable, including respiratory diseases such as asthma, bronchoconstriction, lung inflammation and allergies and the like. Both Ubiquinones and DHEA inhibit NADPH levels in a statistically significant manner, when compared to a control. Moreover, the Ubiquinone inhibits NADPH levels to a similar extent as DHEA. The present invention is broadly applicable to the use of Epiandrosterones (EAs) and Ubiquinones (CoQs) to the treatment of respiratory and lung diseases, and other diseases associated with varying levels of adenosine, adenosine hypersensitivity, asthma, bronchoconstriction, and/or lung inflammation and allergies. The

DHEA and Ubiquinones employed in the present experiments are equivalent to those described and exemplified above.

**Enzymatic assay of purified G6PDH**

The reaction mixture contained 50mM glycyl glycine buffer, pH 7.4, 2 mM D-glucose-6-phosphate, 0.67 mM Beta-NADP, 10 mM MgCL2 and 0.0125 units of G6PDH in a final volume of 3.0 ml. All experiments were repeated 4 times.

The control group contained 3 samples that were added no DHEA or Ubiquinone. The experimental group contained a similar number of samples (3) for each concentration of DHEA or Ubiquinone. One group was added DHEA (in triplicate) at different concentrations. A second group was added different concentrations of a CoQ of long side chain (in triplicate), and a third group received a CoQ of short side chain (in triplicate), both at various doses in the  $\mu$ M range.

The reaction was started by addition of the enzyme, and the increase in absorbance at 340 nm was measured for 5 minutes. Each data point was conducted in triplicate, and the full experiment was repeated 4 times.

Both DHEA and the Ubiquinones inhibited the enzyme activity in a statistically significant manner when compared to controls. DHEA was found to inhibit by 72% in vitro the activity of purified G6PDH when compared to control. Both Ubiquinones inhibited the activity of purified G6PDH in vitro by an amount that was not statistically significantly different from that of DHEA. Both DHEA and the Ubiquinones inhibited the enzyme in a statistically significant manner when compared to controls. Both long chain and short chain CoQs were found to be effective inhibitors of G6PDH.

The above results clearly indicate that CoQ reduced cellular levels of NADPH to an extent similar to DHEA and consequently cellular adenosine levels, and has a therapeutic effect on diseases and conditions associated with them. The present results show that CoQs have a therapeutic effect similar to that of epiandrosterones. The pathways involved in the present invention, as described above, show the criticality of the results reported here, showing that an Epiandrosterone (DHEA) and two Ubiquinones inhibit NADPH levels in a statistically significant manner. The same epiandrosterone (DHEA) was shown in Examples 1 and 2 to decrease levels of adenosine in various tissues. The two different Ubiquinones employed lowered NADPH levels to a similar extent as DHEA. The NADPH reduction caused by the Ubiquinones will, in the case of DHEA, result in lower cellular adenosine levels or adenosine depletion. Thus, in accordance with the invention, both Epiandrosterones and Ubiquinones decrease levels of adenosine and are, therefore, useful in the therapy of diseases and conditions where a decrease of adenosine levels or its depletion are desirable, including respiratory and airway diseases such as asthma, bronchoconstriction, lung inflammation and allergies, and the like.

These are clearly superior results, which could not have been expected based on the knowledge of the art at the time of this invention. The experimental data and results provided are clearly enabling of the effect of ubiquinones on adenosine cellular levels and, therefore, on its therapeutic affect on diseases and conditions associated with them, as described and claimed in this patent.

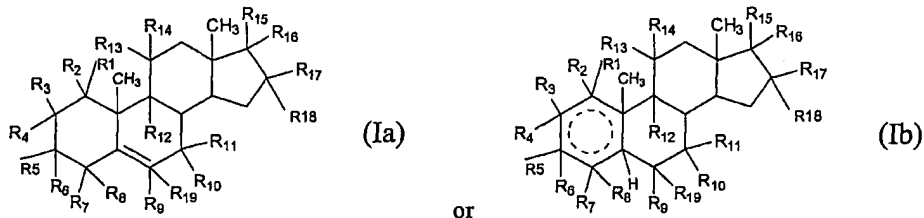
The foregoing examples are illustrative of the present invention, and are not to be construed as limiting thereof. The invention is defined by the following claims, with equivalents of the claims to be included therein.



**WHAT IS CLAIMED AS NOVEL & UNOBVIOUS****IN UNITED STATES LETTERS PATENT IS:**

1. A pharmaceutical composition, comprising a pharmaceutically or veterinarily acceptable carrier or diluent, and prophylactic or therapeutic amounts of a first and second active agents;

the first active agent comprising an oligonucleotide(s) (oligo(s)) that is anti-sense to the initiation codon, the coding region, the 5'-end or the 3'-end genomic flanking regions, the 5' and 3' intron-exon junctions, or regions within 2 to 10 nucleotides of the junctions of one or more gene(s) encoding or to regulatory sequence(s) associated with one or more target polypeptide(s) associated with lung and/or nasal airway dysfunction, or anti-sense to the corresponding mRNA; or combinations or mixtures of the oligo(s); and the second active agent comprising an anti-inflammatory steroid (AIS) of chemical formula

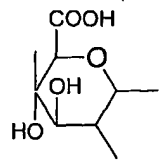


wherein  $R_1, R_2, R_3, R_4, R_6, R_7, R_8, R_9, R_{10}, R_{12}, R_{13}, R_{14}$  and  $R_{19}$  are independently H, OR, halogen,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkyne,  $(C_1-C_{10})$  alkoxy, or two or more of  $R_1, R_2, R_3, R_4, R_6, R_7, R_8, R_9, R_{10}, R_{12}, R_{13}, R_{14}$  and  $R_{19}$  can be linked by combination of the atoms of C, O, N, S, P and Si to form a 3 to 15 member ring(s), in the  $\alpha$ - and/or  $\beta$ - configuration;

$R_5, R_6, R_{10}$ , and  $R_{11}$  are independently OH, SH, H, halogen, pharmaceutically acceptable ester, pharmaceutically acceptable thioester, pharmaceutically acceptable ether, pharmaceutically acceptable thioether, pharmaceutically acceptable inorganic esters, pharmaceutically acceptable monosaccharide, disaccharide or oligosaccharide, spirooxirane, spirothirane,  $-OSO_2R_{20}$ ,  $-OPOR_{20}R_{21}$ ,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkyne or  $OR_{23}$ ,  $-SO_2O-CH_2CHCH_2OCOR_{25}$

wherein,  $R_{23}$  is hydrogen or  $SO_2OM$ , wherein M is selected from H, Na, sulfatide;

$-PO_2O-CH_2CHCH_2OCOR_{25}$   
phosphatide  $OCOR_{24}$ , wherein  $R_{24}$  and  $R_{25}$ , which may be the same or different, are straight or branched  $(C_1-C_{20})$  alkyl,  $(C_1-C_{20})$  alkene,  $(C_1-C_{20})$  alkyne, sugar, polyethyleneglycol (PEG) or glucuronide



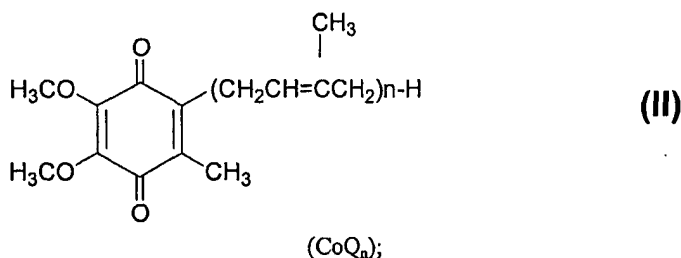
$R_5$  and  $R_6$  taken together are  $=O$ ;

$R_{10}$  and  $R_{11}$  taken together are  $=O$ ;

$R_{15}$  is (1) H, halogen,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkyne, or  $(C_1-C_{10})$  alkoxy when  $R_{16}$  is  $-C(O)OR_{22}$ , (2) H, halogen, OH,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene or  $(C_1-C_{10})$  alkyne, when  $R_{16}$  is halogen, OH,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene or  $(C_1-C_{10})$  alkyne, (3) H, halogen,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkenyl,  $(C_1-C_{10})$  alkynyl, formyl,  $(C_1-C_{10})$  alkanoyl or epoxy when  $R_{16}$  is OH, (4) OR, SR, SH, H, halogen, pharmaceutically acceptable ester, pharmaceutically acceptable thioester, pharmaceutically acceptable ether, pharmaceutically acceptable thioether, pharmaceutically acceptable inorganic esters, pharmaceutically acceptable monosaccharide, disaccharide or oligosaccharide, spirooxirane, spirothirane,  $-OSO_2R_{20}$  or  $-OPOR_{20}R_{21}$  when  $R_{16}$  is H, or  $R_{15}$  and  $R_{16}$  taken together are  $=O$ ;

$R_{17}$  and  $R_{18}$  are independently (1) H, -OH, halogen,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkyne or  $-(C_1-C_{10})$  alkoxy when  $R_6$  is H OR, halogen,  $(C_1-C_{10})$  alkyl or  $-C(O)OR_{22}$ , (2) H,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  amino,  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkyne,  $((C_1-C_{10})$  alkyl),  $((C_1-C_{10})$  amino- $(C_1-C_{10})$  alkyl,  $((C_1-C_{10})$  alkene),  $((C_1-C_{10})$  amino- $(C_1-C_{10})$  alkyl,  $((C_1-C_{10})$  alkyne),  $((C_1-C_{10})$  amino- $(C_1-C_{10})$  alkyl,  $((C_1-C_{10})$  alkyl),  $((C_1-C_{10})$  amino- $(C_1-C_{10})$  alkene,  $((C_1-C_{10})$  alkene),  $((C_1-C_{10})$  amino- $(C_1-C_{10})$  alkene,  $((C_1-C_{10})$  alkyne),  $((C_1-C_{10})$  amino- $(C_1-C_{10})$  alkyne,  $((C_1-C_{10})$  alkene),  $((C_1-C_{10})$  amino- $(C_1-C_{10})$  alkyne,  $((C_1-C_{10})$  alkyne),  $((C_1-C_{10})$  amino- $(C_1-C_{10})$  alkyne,  $(C_1-C_{10})$  alkoxy, hydroxy -  $(C_1-C_{10})$  alkyl, hydroxy -  $(C_1-C_{10})$  alkene, hydroxy -  $(C_1-C_{10})$  alkyne,  $(C_1-C_{10})$  alkoxy -  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkoxy -  $(C_1-C_{10})$  alkene,  $(C_1-C_{10})$  alkoxy -  $(C_1-C_{10})$  alkyne, (halogen) $_m$   $(C_1-C_{10})$  alkyl, (halogen) $_m$   $(C_1-C_{10})$  alkene, (halogen) $_m$   $(C_1-C_{10})$  alkyne,  $(C_1-C_{10})$  alkanoyl, formyl,  $(C_1-C_{10})$  carbalkoxy or  $(C_1-C_{10})$  alkanoyloxy when  $R_{15}$  and  $R_{16}$  taken together are =O, (3)  $R_{17}$  and  $R_{18}$  taken together are =O; (4)  $R_{17}$  and  $R_{18}$  taken together with the carbon to which they are attached form a 3-6 member ring containing 0 or 1 oxygen atom; or (5)  $R_{15}$  and  $R_{17}$  taken together with the carbons to which they are attached form an epoxide ring;  $R_{20}$  and  $R_{21}$  are independently OH, pharmaceutically acceptable ester or pharmaceutically acceptable ether;  $R_{22}$  is H, (halogen) $_m$   $(C_1-C_{10})$  alkyl, (halogen) $_m$   $(C_1-C_{10})$  alkene, (halogen) $_m$   $(C_1-C_{10})$  alkyne,  $(C_1-C_{10})$  alkyl,  $(C_1-C_{10})$  alkene or  $(C_1-C_{10})$  alkyne; n is 0, 1 or 2; and m is 1, 2 or 3, ; or pharmaceutically or veterinarily acceptable salts thereof; and/or

a ubiquinone of the chemical formula



wherein  $n=1$  to 12, or pharmaceutically or veterinarily acceptable salts thereof; the first and second agents being present in amounts effective for reducing or depleting levels of, or reducing sensitivity to, adenosine, reducing levels of adenosine receptors, producing bronchodilation, increasing levels of ubiquinone or lung surfactant in a subject's tissue (s), or treating bronchoconstriction, lung inflammation or lung allergies or a respiratory or lung disease or condition.

2. The composition of claim 1, wherein the oligo contains up to about 15% A.

3. The composition of claim 1, wherein the oligo(s) of the first active agent is (are) anti-sense to the initiation codon, the coding region, the 5'-end or the 3'-end genomic flanking regions, the 5' or 3' intron-exon junctions, and regions within 2 to 10 nucleotides of the junctions of at least one oncogene(s) or a gene(s) encoding, or regulating expression of, a target polypeptide(s) associated with lung and/or nasal airway dysfunction or cancer, is (are) anti-sense to the corresponding mRNA(s). Multiple target anti-sense oligo(s) (MTAs) or combinations thereof; the polypeptides comprising peptide factors and transmitters, antibodies, cytokines or chemokines, enzymes, binding proteins, adhesion molecules, their receptors, or malignancy associated proteins.

4. The composition of claim 3, wherein the oligo(s) is (are) anti-sense to the initiation codon, the coding region, the 5'-end or the 3'-end genomic flanking regions, the 5' or 3' intron-exon junctions, or regions within 2 to 10 nucleotides of the junctions of at least one oncogene(s) or a gene(s) encoding, or regulating expression of, a target polypeptide(s) associated with lung and/or nasal airway dysfunction or is (are) anti-sense to the oncogene mRNA, or the corresponding mRNA; or MTAs or combinations thereof; wherein the polypeptides comprise of transcription factors, stimulating or activating peptide factors, cytokines, cytokine receptors, chemokines, chemokine receptors, adenosine receptors, bradykinin receptors, endogenously produced specific or non-specific enzymes, immunoglobulins or antibodies, antibody receptors, central nervous system (CNS) or peripheral nervous or non-nervous system receptors, CNS or peripheral nervous or non-nervous system peptide transmitters, adhesion molecules, defensins, growth factors, vasoactive peptides and receptors, binding proteins, or malignancy associated proteins.

5. The composition of claim 4, wherein the encoded polypeptide(s) comprise(s) one or more adenosine receptors  $A_1$ ,  $A_{2a}$ ,  $A_{2b}$  or  $A_3$ , bradykinin receptors B1 or B2, NfκB Transcription Factor, Interleukin-8

Receptor (IL-8 R), Interleukin 5 Receptor (IL-5 R), Interleukin 4 Receptor (IL-4 R), Interleukin 3 Receptor (IL-3 R), Interleukin-1 $\beta$  (IL-1 $\beta$ ), Interleukin 1 $\beta$  Receptor (IL-1 $\beta$  R), Eotaxin, Tryptase, Major Basic Protein,  $\beta$ 2-adrenergic Receptor Kinase, Endothelin Receptor A, Endothelin Receptor B, Preproendothelin, Bradykinin B2 Receptor, IgE High Affinity Receptor, Interleukin 1 (IL-1), Interleukin 1 Receptor (IL-1 R), Interleukin 9 (IL-9), Interleukin-9 Receptor (IL-9 R), Interleukin 11 (IL-11), Interleukin-11 Receptor (IL-11 R), Inducible Nitric Oxide Synthase, Cyclo-oxygenase-1 (COX-1), Cyclo-oxygenase-2 (COX-2), Intracellular Adhesion Molecule 1 (ICAM-1) Vascular Cellular Adhesion Molecule (VCAM), Rantes, Endothelial Leukocyte Adhesion Molecule (ELAM-1), Monocyte Activating Factor, Neutrophil Chemotactic Factor, Neutrophil Elastase, Defensin 1, 2 and 3, Muscarinic Acetylcholine Receptors, Platelet Activating Factor, Tumor Necrosis Factor  $\alpha$ , 5-lipoxygenase, Phosphodiesterase IV, Substance P, Substance P Receptor, Histamine Receptor, Chymase, CCR-1 CC Chemokine Receptor, CCR-2 CC Chemokine Receptor, CCR-3 CC Chemokine Receptor, CCR-4 CC Chemokine Receptor, CCR-5 CC Chemokine Receptor, Prostanoid Receptors, GATA-3 Transcription Factor, Neutrophil Adherence Receptor, MAP Kinase, Interleukin-9 (IL-9), NFAT Transcription Factors, STAT 4, MIP-1 $\alpha$ , MCP-2, MCP-3, MCP-4, Cyclophilins, Phospholipase A2, Basic Fibroblast Growth Factor, Metalloproteinase, CSBP/p38 MAP Kinase, Tryptase Receptor, PDG2, Interleukin-3 (IL-3), Interleukin-1 $\beta$  (IL-1 $\beta$ ), Cyclosporin A-Binding Protein, FK5-Binding Protein,  $\alpha$ 4 $\beta$ 1 Selectin, Fibronectin,  $\alpha$ 4 $\beta$ 7 Selectin, Mad CAM-1, LFA-1 (CD11a/CD18), PECAM-1, LFA-1 Selectin, C3bi, PSGL-1, E-Selectin, P-Selectin, CD-34, L-Selectin, p150,95, Mac-1 (CD11b/CD18), Fucosyl transferase, VLA-4, CD-18/CD11a, CD11b/CD18, ICAM2 and ICAM3, C5a, CCR3 (Eotaxin Receptor), CCR1, CCR2, CCR4, CCR5, LTB-4, AP-1 Transcription Factor, Protein kinase C, Cysteinyl Leukotriene Receptor, Tachychinen Receptors (tach R), I $\kappa$ B Kinase 1 & 2, STAT 6, c-mas or NF-Interleukin-6 (NF-IL-6).

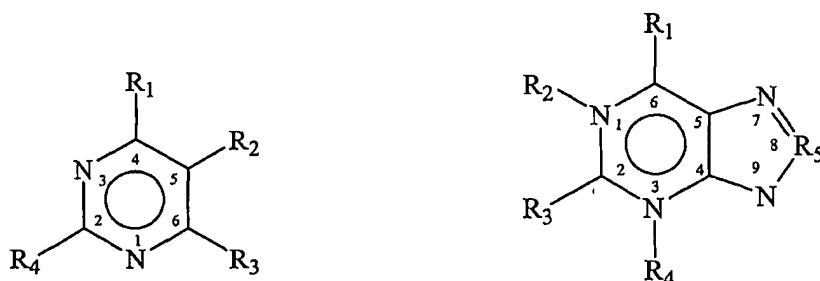
6. The composition of claim 4, wherein the encoded polypeptide(s) comprise(s) a H2A histone family member N, Tubulin, beta polypeptide, ELL gene (11-19 lysine-rich leukemia gene); 7-dehydrocholesterol reductase, ADP-ribosylation factor-like 7, Karyopherin alpha 2 (RAG cohort 1, importin alpha 1), EST (AI038433), EST (AI122689), EST (AI092623), ESTs (AI095492), ESTs (AI138216), ESTs (AI128305), ESTs (AI125228), ESTs (AI041482), ESTs (AI051839), Homo sapiens mRNA; cDNA DKFZp434A1716, ESTs (AI096522), ESTs (AI122807), ESTs (AI041212), EST (AI125651), Enolase 1, (alpha), EST (AI024215), EST (AI034360), Homo sapiens mRNA; cDNA DKFZp564H0764, Homo sapiens mRNA for KIAA1363 protein, partial cds, Potassium voltage-gated channel, shaker-related subfamily, beta member 2, ER-associated DNAJ; ER-associated Hsp40 co-chaperone; hDj9; ERj3, ESTs, Weakly similar to p38 protein [H.sapiens] (AA906703), CGI-142, ESTs (AA463249), Homo sapiens clone 25058 mRNA sequence ESTs (R49144), Squamous cell carcinoma antigen 1, ESTs (AA425700), Myosin X, ESTs (AA459692), Epithelial protein lost in neoplasm beta, CD44 antigen (homing function and Indian blood group system), Coagulation factor III (thromboplastin, tissue factor), ESTs (AA909635), Adducin 1 (alpha), 5' Nucleotidase (CD73), ESTs, moderately similar to semaphorin C [M.musculus] (AA293300), ESTs (AA278764), ESTs (AA678160), Calmodulin 2 (phosphorylase kinase, delta), ESTs (R42770), Chloride intracellular channel 1, High-mobility group (nonhistone chromosomal) protein 17, Ubiquitin carrier protein, Tubulin, alpha 1 (testis specific), Transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase), Sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican), Proteasome (prosome, macropain) 26S subunit, non-ATPase, 2, Tubulin, beta polypeptide, Filamin B, beta (actin-binding protein-278), Stanniocalcin, Low density lipoprotein receptor (familial hypercholesterolemia), Plectin 1, intermediate filament binding protein, 500kD, S100 calcium-binding protein A2, Immediate early response 3, Calpain, large polypeptide L2, Pleckstrin homology-like domain, family A, member 1, Melanoma adhesion molecule, CD44 antigen (homing function and Indian blood group system), Programmed cell death 5, Hexokinase 1, Vascular endothelial growth factor, Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor), Calumenin, Syntaxin 11, Diphtheria toxin receptor (heparin-binding epidermal growth factor-like growth factor), Fn14 for type I transmembrane protein, Nef-associated factor 1, High-mobility group (nonhistone chromosomal) protein isoforms I and Y, Catechol-O-methyltransferase, C-terminal binding protein 1, Collagen, type XVII, alpha 1, ESTs (N58473), Farnesyl-diphosphate farnesyltransferase 1 RNA helicase-related protein, Interferon stimulated gene (20kD), Steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1), Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase), Laminin, alpha 3 (nicotin (150kD), kalinin (165kD), BM600 (150kD), epilegrin), Collagen, type XVII, alpha 1, Keratin 18, Heparan sulfate (glucosamine) 3-O-sulfotransferase 1, Tubulin, alpha 2, Adenylyl cyclase-associated protein, Forkhead box D1, Cathepsin C, ESTs, Highly similar to AF151802\_1 CGI-44 protein [H.sapiens] (T74688), Ribonucleotide reductase

M2 polypeptide, Laminin, gamma 2 (nicein (100kD), kalinin (105kD), BM600 (100kD), Herlitz junctional epidermolysis bullosa)), Homo sapiens mRNA; cDNA DKFZp586P1622 (from clone DKFZp586P1622), ESTs, Weakly similar to /prediction (AA284245), or Lactate dehydrogenase A.

7. The composition of claim 1, wherein one or more As of the first active agent is(are) substituted by a universal base comprising a heteroaromatic base that binds to thymidine or uridine but has antagonist activity or less than about 0.3 of the adenosine agonist or antagonist activity at the adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub> or A<sub>3</sub> receptors.

8. The composition of claim 7, wherein the heteroaromatic base(s) comprise(s) pyrimidines or purines, which may be substituted by O, halo, NH<sub>2</sub>, SH, SO, SO<sub>2</sub>, SO<sub>3</sub>, COOH, branched or fused primary or secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, arylcycloalkyl, all of which may be further substituted by O, halo, NH<sub>2</sub>, primary, secondary or tertiary amine, SH, SO, SO<sub>2</sub>, SO<sub>3</sub>, cycloalkyl, heterocycloalkyl or heteroaryl.

9. The composition of claim 7, wherein the purines are substituted at positions 1, 2, 3, 6, and/or 8, the pyrimidines are substituted at positions 2, 3, 4, 5 and/or 6, and the purines and pyrimidines have the chemical formula



pyrimidines

or

purines

wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> and R<sup>5</sup> are independently H, alkyl, alkenyl or alkynyl and R<sup>3</sup> is H, aryl, dicycloalkyl, dicycloalkenyl, dicycloalkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, O-cycloalkyl, O-cycloalkenyl, O-cycloalkynyl, NH<sub>2</sub>-alkylamino-ketoxyalkoxy-aryl, or mono or dialkylaminoalkyl-N-alkylamino-SO<sub>2</sub>aryl, and R<sub>4</sub> and R<sub>5</sub> are independently R<sub>1</sub> and together are R<sub>3</sub>, and the pyrimidines and purines optionally comprise theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline or xanthine.

10. The composition of claim 9, wherein the universal base of the first active agent comprises 3-nitropyrrole-2'-deoxynucleoside, 5-nitro-indole, 2-deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5-nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3,4-dihydropyrimido [4,5-c] oxazine-7-one or 2-amino-6-methoxyaminopurine.

11. The composition of claim 1, wherein if present in the first active agent(s), one or more methylated cytosine(s) (<sup>m</sup>C) is(are) substituted for a C in or to form one or more CpG dinucleotide(s).

12. The composition of claim 1, wherein one or more mononucleotide(s) of the first active agent(s) is(are) linked or modified by one or more of methylphosphonate, 5'-N-carbamate, phosphotriester, phosphorothioate, phosphorodithioate, boranophosphate, formacetal, thioformacetal, thioether, carbonate, carbamate, sulfate, sulfonate, sulfamate, sulfonamide, sulfone, sulfite, sulfoxide, sulfide, hydroxylamine, methylene(methylimino) (MMI), methoxymethyl (MOM), methoxyethyl (MOE), methyleneoxy (methylimino) (MOMI), 2'-O-methyl, phosphoramidate, or C-5 substituted residues.

13. The composition of claim 12, wherein one or more mononucleotide residue(s) of the first active agent(s) are linked by phosphorothioate residues.

14. The composition of claim 1, wherein the anti-sense oligo of the first active agent(s) comprise(s) about 7 to about 60 mononucleotides.

15. The composition of claim 1, wherein the anti-sense oligo of the first active agent(s) comprise(s) fragments 1, 3, 5, 7 and 8 to 2498 (SEQ ID NOS: 1 through 2498).

16. The composition of claim 1, wherein the anti-sense oligo of the first active agent(s) is(are) operatively linked to, or complexed with, a cell internalized or up-taken agent(s) or a cell targeting agent(s).

17. The composition of claim 15, wherein the cell internalized or up-taken agent comprises transferrin, asialoglycoprotein or streptavidin, and the cell targeting agent comprises a prokaryotic or eukaryotic vector or plasmid.

18. The composition of claim 1, wherein the oligo contains up to about 10% A.

19. The composition of claim 1, wherein the oligo(s) of the first active agent(s) is(are) hybridized to a ribonucleic acid or a deoxyribonucleic acid and delivered as a double stranded agent.

20. The composition of claim 1, wherein the carrier or diluent comprises a gaseous, liquid, or solid carrier or diluent, and the active agents are present in an amount of about 0.01 to about 99.99 w/w of the composition.

21. The composition of claim 20, further comprising an agent selected from other therapeutic agents, surfactants, flavoring or coloring agents, fillers, volatile oils, buffering agents, dispersants, RNA inactivating agents, anti-oxidants, flavoring agents, propellants or preservatives.

22. The composition of claim 21, wherein the other therapeutic or bioactive agent(s) is (are) selected from analgesics, pre-menstrual medications, menopausal agents, anti-aging agents, anti-anxiolytic agents, mood disorder agents, anti-depressants, anti-bipolar mood agents, anti-schizophrenic agents, anti-cancer agents, alkaloids, blood pressure controlling agents, muscle relaxants, steroids, soporific agents, anti-ischemic agents, anti-arrhythmic agents, contraceptives, vitamins, minerals, tranquilizers, neurotransmitter regulating agents, wound healing agents, anti-angiogenic agents, cytokines, growth factors, B-adrenergic receptor agonists, anti-metastatic agents, antacids, anti-histaminic agents, anti-bacterial agents, anti-viral agents, anti-gas agents, appetite suppressants, sun screens, emollients, skin temperature lowering products, radioactive phosphorescent or fluorescent contrast diagnostic or imaging agents, libido altering agents, bile acids, laxatives, anti-diarrheic agents, skin renewal agents, hair growth agents, analgesics, pre-menstrual medications, anti-menopausal agents, hormones, anti-aging agents, anti-anxiolytic agents, nociceptive agents, mood disorder agents, anti-depressants, anti-bipolar mood agents, anti-schizophrenic agents, anti-cancer agents, alkaloids, blood pressure controlling agents, other hormones, other anti-inflammatory agents, agents for treating arthritis, burns, wounds, chronic bronchitis, chronic obstructive pulmonary disease (COPD), inflammatory bowel disease such as Crohn's disease, ulcerative colitis, autoimmune disease, or lupus erythematosus, muscle relaxants, soporific agents, anti-ischemic agents, anti-arrhythmic agents, contraceptives, vitamins, minerals, tranquilizers, neurotransmitter regulating agents, wound and burn healing agents, anti-angiogenic agents, cytokines, growth factors, anti-metastatic agents, antacids, anti-histaminic agents, anti-bacterial agents, anti-viral agents, anti-gas agents, agents for reperfusion injury, counteracting appetite suppressants, sun screens, emollients, skin temperature lowering products, radioactive phosphorescent or fluorescent contrast diagnostic or imaging agents, libido altering agents, bile acids, laxatives, anti-diarrheic agents, skin renewal agents or hair growth agents.

23. The composition of claim 22, wherein the surfactant comprises surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D and surfactant Protein E, di-saturated phosphatidyl choline (other than dipalmitoyl), dipalmitoyl phosphatidyl choline, phosphatidyl choline, phosphatidyl glycerol, phosphatidyl inositol, phosphatidyl ethanolamine, phosphatidyl serine; phosphatidic acid, ubiquinones, lysophosphatidyl ethanolamine, lysophosphatidyl choline, palmitoyl-lysophosphatidyl choline, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxy acetone, palmitate, cytidine diphosphate (CDP) diacyl glycerol, CDP choline, choline, choline phosphate; natural or artificial lamellar bodies as carrier surfactant vehicles, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitinic acid, non-ionic block copolymers of ethylene or propylene oxides, polyoxypropylene, monomeric or polymeric, polyoxyethylene, monomeric and polymeric, poly (vinyl amine) with dextran and/or alkanoyl side chains, Brij 35, Triton X-100 or synthetic surfactants ALEC, Exosurf, Survan or Atovaquone.

24. The composition of claim 1, comprising one or more oligo(s), an anti-inflammatory steroid(s) of formula (Ia) or (Ib), a steroid, a surfactant, and a carrier or diluent for the oligo.

25. The composition of claim 1, wherein the second active agent comprises  $\text{CoQ}_n$ , wherein n is 1 to 10.

26. The composition of claim 1, wherein the second active agent comprises  $\text{CoQ}_n$ , wherein n is 6 to

10.

27. The composition of claim 1, wherein the second active agent comprises  $\text{CoQ}_n$ , wherein  $n$  is 10.
28. The composition of claim 1, wherein the second active agent comprises an anti-inflammatory steroid (AIS) of formula (Ia) selected from dehydroepiandrosterone, wherein  $R$  and  $R^1$  are H and the broken line represents a double bond, 16-alpha bromodehydroepiandrosterone wherein  $R$  is Br,  $R^1$  is H and the broken line represents a double bond, 16-alpha fluorodehydroepiandrosterone wherein  $R$  is F,  $R^1$  is H and the broken line represents a double bond, etiocholanolone, wherein  $R$  and  $R^1$  are each hydrogen and the broken line represents a single bond, dehydroepiandrosterone sulfate, wherein  $R$  is H,  $R^1$  is  $\text{SO}_2\text{OM}$  and  $M$  is a sulfatide group as defined above, and the broken line represents a double bond, the compound of formula (Ia),  $R$  is halogen selected from Br, Cl or F,  $R^1$  is H, and the broken line represents a double bond, 16-alpha-fluorodehydro-epiandrosterone, or pharmaceutically or veterinarily acceptable salts thereof.
29. The composition of claim 1, wherein the oligo(s) of the first agent contains up to about 5% A.
30. The composition of claim 1, wherein the oligo(s) of the first agent is A free.
31. The composition of claim 1, wherein the second active agent comprises an anti-inflammatory steroid (AIS) of formula (Ib), wherein  $R^{15}$  and  $R^{16}$  together are  $=\text{O}$ ;  $R^5$  is  $-\text{OH}$ ;  $R^5$  is  $-\text{OSO}_2\text{R}^{20}$ ;  $R^{15}$  and  $R^{20}$  together is H; or pharmaceutically or veterinarily acceptable salts thereof.
32. The composition of claim 1, wherein the second active agent comprises an AIS selected from budesonide, testosterone, progesterone, fluticasone, beclomethasone, prednisone, mometasone, estrogen, dexamethasone, hydrocortisone, triamcinolone, flunisolide, methylprednisolone prednisone, hydrocortisone, or analogues thereof.
33. The composition of claim 1, wherein the active agents are present in an amount of about 0.01 to about 99.99 w/w of the composition.
34. The composition of claim 1, wherein the second active agent comprises an anti-inflammatory steroid (AIS) selected from 21-acetoxypregnenolone ((3 $\beta$ )-21-(acetyloxy)-3-hydroxypregn-5-en-20-one); alclometasone ((7 $\alpha$ , 11 $\beta$ , 16 $\alpha$ )-7-Chloro-11, 17, 21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), or its 17,21-dipropionate form ( $\text{C}_{28}\text{H}_{37}\text{ClO}_7$ ); algestone ((16 $\alpha$ )-16,17-dihydroxypregn-4-ene-3,20-dione), its cyclic acetal with acetone form ( $\text{C}_{24}\text{H}_{34}\text{O}_4$ ), or its 16 $\alpha$ -methyl ether form ( $\text{C}_{22}\text{H}_{32}\text{O}_4$ ); amcinonide ((11 $\beta$ , 16 $\alpha$ )-21-(acetyloxy)-16,17-[cyclopentylidenebis(oxy)]-9-fluoro-11-hydroxypregna-1,4-di-ene-3,20-dione); beclomethasone ((11 $\beta$ , 16 $\beta$ )-9-chloro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its dipropionate form ( $\text{C}_{28}\text{H}_{37}\text{ClO}_7$ ), or its monopropionate form; betamethasone ((11 $\beta$ , 16 $\beta$ )-9-fluoro-11, 17, 21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $\text{C}_{24}\text{H}_{31}\text{FO}_6$ ), its 21-adamantoate form ( $\text{C}_{33}\text{H}_{43}\text{FO}_6$ ), its 17-benzoate form ( $\text{C}_{29}\text{H}_{33}\text{FO}_6$ ), its 17, 21-dipropionate form ( $\text{C}_{28}\text{H}_{37}\text{FO}_7$ ), its 17-valerate form ( $\text{C}_{27}\text{H}_{37}\text{FO}_6$ ), or its 21-phosphate disodium salt form ( $\text{C}_{22}\text{H}_{28}\text{FNa}_2\text{O}_8\text{P}$ ); budesonide ((11 $\beta$ , 16 $\alpha$ )-16,17-[butylidenebis(oxy)]-11, 21-dihydropregna-1,4-diene-3,20-dione); chloroprednisone ((6 $\alpha$ )-chloro-17,21-dihydroxypregna-1,4-diene-3,11,20-trione), or its 21-acetate form ( $\text{C}_{23}\text{H}_{27}\text{ClO}_6$ ); ciclesonide; clobetasol ((11 $\beta$ , 16 $\beta$ )-21-chloro-9-fluoro-11,17-dihydroxy-16-methylpregna-1,4-diene-3,20-dione), or its 17-propionate form ( $\text{C}_{25}\text{H}_{32}\text{ClFO}_5$ ); clobetasone ((16 $\beta$ )-21-chloro-9-fluoro-17-hydroxy-16-methylpregna-1,4-diene-3,11,20-trione), or its 17-butyrate form ( $\text{C}_{26}\text{H}_{32}\text{ClFO}_5$ ); clocortolone ((6 $\alpha$ , 11 $\beta$ , 16 $\alpha$ )-9-chloro-6-fluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $\text{C}_{24}\text{H}_{30}\text{ClFO}_5$ ), or its 21-pivalate form ( $\text{C}_{27}\text{H}_{36}\text{ClFO}_5$ ); cloprednol ((11 $\beta$ )-6-chloro-11,17,21-trihydroxypregna-1,4,6-triene-3,20-dione); coroxon (phosphoric acid 3-chloro-4-methyl-2-oxo-2H-1-benzopyran-7-yl diethyl ester); cortisone (17,21-dihydroxypregn-4-ene-3,11,20-trione), its 21-acetate form ( $\text{C}_{23}\text{H}_{30}\text{O}_6$ ), or its 21-cyclopentanepropionate form ( $\text{C}_{29}\text{H}_{40}\text{O}_6$ ); cortivazol ((11 $\beta$ , 16 $\alpha$ )-21-(acetyloxy)-11,17-dihydroxy-6,16-dimethyl-2'-phenyl-2'-H-pregna-2,4,6-trieno[3,2-c]pyrazol-20-one); deflazacort ((11 $\beta$ , 16 $\beta$ )-21-(acetyloxy)-11-hydroxy-2'-methyl-5'-H-pregna-1,4-dieno[17,16-d]oxazole-3,20-dione); desonide ((11 $\beta$ , 16 $\alpha$ )-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); desoximetasone ((11 $\beta$ , 16 $\alpha$ )-9-fluoro-11, 21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione); dexamethasone ((11 $\beta$ , 16 $\alpha$ )-9-fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $\text{C}_{24}\text{H}_{31}\text{FO}_6$ ), its 21-(3,3-dimethylbutyrate) form ( $\text{C}_{28}\text{H}_{39}\text{FO}_6$ ; Chemerda et al., US Patent No. 2,939,873), its 21-diethylaminoacetate form ( $\text{C}_{28}\text{H}_{41}\text{FNO}_6$ ), its 21-isonicotinate form ( $\text{C}_{28}\text{H}_{41}\text{FNO}_6$ ), its 17,21-dipropionate form ( $\text{C}_{28}\text{H}_{37}\text{FNO}_6$ ), or its 21-palmitate form ( $\text{C}_{38}\text{H}_{59}\text{FO}_6$ ); diflorasone ((6 $\alpha$ , 11 $\beta$ , 16 $\beta$ )-6,9-difluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), or its diacetate form ( $\text{C}_{26}\text{H}_{32}\text{F}_2\text{O}_7$ ); diflucortolone ((6 $\alpha$ , 11 $\beta$ , 16 $\alpha$ )-6,9-difluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione),

or its 21-valerate form ( $C_{27}H_{36}F_2O_5$ ); difluprednate ((6 $\alpha$ ,11 $\beta$ )-21-(acetyloxy)-6,9-difluoro-11-hydroxy-17-(1-oxobutoxy)pregna-1,4-diene-3,20-dione); enoxolone ((3 $\beta$ ,20 $\beta$ )-3-hydroxy-11-oxoolean-12-en-29-oic acid), or its 18 $\alpha$ -hydrogen form; fluazacort ((11 $\beta$ ,16 $\beta$ )-21-(acetyloxy)-9-fluoro-11-hydroxy-2'-methyl-5'H-pregna-1,4-dieno[17,16-d]oxazole-3,20-dione); flucoronide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-9,11-dichloro-6-fluoro-21-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); flumethasone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6,9-difluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{24}H_{30}F_2O_6$ ), or its 21-pivalate form ( $C_{27}H_{36}F_2O_6$ ); flunisolide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene) bis(oxy)]pregna-1,4-diene-3,20-dione), or its 21-acetate form ( $C_{26}H_{33}FO_7$ ); fluocinolone acetate ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); fluocinonide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-21-(acetyloxy)-6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); fluocortin butyl ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11-hydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-oic acid butyl ester); fluocortolone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{24}H_{31}FO_5$ ), its 21-hexanoate form ( $C_{28}H_{39}FO_5$ ), or its 21-pivalate form ( $C_{22}H_{37}FO_5$ ); fluorometholone ((6 $\alpha$ ,11 $\beta$ )-9-fluoro-11,17-dihydroxy-6-methylpregna-1,4-diene-3,20-dione), or its 17-acetate form ( $C_{24}H_{31}FO_5$ ); fluperolone acetate ((11 $\beta$ ,17 $\alpha$ ,17(S))-17-[2-(acetyloxy)-1-oxopropyl]-9-fluoro-11,17-dihydroxyandrost-1,4-dien-3-one); fluprednidene acetate ((11 $\beta$ )-21-(acetyloxy)-9-fluoro-11,17-dihydroxy-16-methylenepregna-1,4-diene-3,20-dione); fluprednisolone ((6 $\alpha$ ,11 $\beta$ )-6-fluoro-11,17,21-trihydroxypregna-1,4-diene-3,20-dione), or its 21-acetate form ( $C_{23}H_{29}FO_6$ ); flurandrenolide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregn-4-ene-3,20-dione); fluticasone propionate ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ ,17 $\alpha$ )-6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)androst-1,4-diene-17-carbothioic acid S-(fluoromethyl) ester); formocortal ((11 $\beta$ ,16 $\alpha$ )-21-(acetyloxy)-3-(2-chloroethoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-20-oxopregna-3,5-diene-6-carboxaldehyde); halcinonide ((11 $\beta$ ,16 $\alpha$ )-21-chloro-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregn-4-ene-3,20-dione); halobetasol propionate (6 $\alpha$ ,11 $\beta$ ,16 $\beta$ )-21-chloro-6,9-difluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)pregna-1,4-diene-3,20-dione); halometasone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-2-chloro-6,9-difluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), or its monohydrate form ( $C_{22}H_{27}ClF_2O_5 \cdot H_2O$ ); halopredone acetate ((6 $\beta$ ,11 $\beta$ )-17,21-bis(acetyloxy)-2-bromo-6,9-difluoro-11-hydroxypregna-1,4-diene-3,20-dione); hydrocortamate (N,N-diethylglycine (11 $\beta$ )-11,17-dihydroxy-3,20-dioxopregn-4-en-21-yl ester), or its hydrochloride form ( $C_{27}H_{41}NO_6 \cdot HCl$ ); hydrocortisone ((11 $\beta$ )-11,17,21-trihydroxypregn-4-ene-3,20-dione), its 21-acetate form ( $C_{23}H_{32}O_6$ ), its 17-butyrate form ( $C_{25}H_{36}O_6$ ), its 21-phosphate disodium salt form ( $C_{21}H_{29}Na_2O_8P$ ), its 21-sodium succinate form ( $C_{25}H_{33}NaO_8$ ), its 17-valerate form ( $C_{26}H_{38}O_6$ ), or its cypionate form; loteprednol etabonate ((11 $\beta$ ,17 $\alpha$ )-17-[(ethoxycarbonyl)oxy]-11-hydroxy-3-oxoandrost-1,4-diene-17-carboxylic acid chloromethyl ester); mazipredone ((11 $\beta$ )-11,17-dihydroxy-21-(4-methyl-1-piperazinyl)pregna-1,4-diene-3,20-dione), or its hydrochloride form ( $C_{26}H_{38}N_2O_4 \cdot HCl$ ); medrysone ((6 $\alpha$ ,11 $\beta$ )-11-hydroxy-6-methylpregn-4-ene-3,20-dione); meprednisone ((16 $\beta$ )-17,21-dihydroxy-16-methylpregna-1,4-diene-3,11,20-trione), or its 21-acetate form ( $C_{24}H_{30}O_6$ ); methylprednisolone ((6 $\alpha$ ,11 $\beta$ )-11,17,21-trihydroxy-6-methylpregna-1,4-diene-3,20-dione; Sebek and Spero, US Patent No. 2,897,218, and Gould, US Patent No. 3,053,832), its 21-acetate form ( $C_{24}H_{32}O_6$ ), its 21-phosphate disodium salt form ( $C_{22}H_{29}Na_2O_8P$ ), its 21-succinate sodium salt form ( $C_{26}H_{33}NaO_8$ ), or its aceponate form ( $C_{27}H_{36}O_7$ ); mometasone furoate ((11 $\beta$ ,16 $\alpha$ )-9,21-dichloro-17-[(2-furanylcarbonyl)oxy]-11-hydroxy-16-methylpregna-1,4-diene-3,20-dione); paramethasone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{24}H_{31}FO_6$ ), its disodium phosphate form, or a mixture of its 21-acetate and disodium phosphate form; prednicarbate ((11 $\beta$ )-17[(ethoxycarbonyl)oxy]-11-hydroxy-21-(1-oxopropoxy)pregna-1,4-diene-3,20-dione); prednisolone ((11 $\beta$ )-11,17,21-trihydroxypregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{23}H_{30}O_6$ ), its 21-*tert*-butylacetate form ( $C_{27}H_{38}O_6$ ; Sarrett), its 21-hydrogen succinate form ( $C_{25}H_{32}O_8$ ), its 21-succinate sodium salt form ( $C_{25}H_{31}NaO_8$ ), its 21-stearoylglycolate form ( $C_{41}H_{64}O_8$ ), its 21-*m*-sulfobenzoate sodium salt form ( $C_{28}H_{31}NaO_9S$ ; (11 $\beta$ )-11,17-dihydroxy-21-[(3-sulfobenzoyl)oxy]pregna-1,4-diene-3,20-dione monosodium salt), or its 21-trimethylacetate form ( $C_{26}H_{36}O_6$ ); prednisolone 21-diethylaminoacetate (N,N-diethylglycine (11 $\beta$ )-11,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl ester; British Patent No. 862,370), or its hydrochloride form ( $C_{27}H_{39}NO_6 \cdot HCl$ ); prednisolone sodium phosphate (11,17-dihydroxy-21-(phosphonoxy)pregna-1,4-diene-3,20-dione disodium salt); prednisone (17,21-dihydroxypregna-1,4-diene-3,11,20-trione), or its 21-acetate form ( $C_{23}H_{28}O_6$ ); prednival ((11 $\beta$ )-11,21-dihydroxy-17-[(1-oxopentyl)oxy]pregna-1,4-



diene-3,20-dione;), or its 21-acetate form ( $C_{28}H_{38}O_7$ ); prednylidene ((11 $\beta$ )-11,17,21-trihydroxy-16-methylenepregna-1,4-diene-3,20-dione), or its 21-diethylaminoacetate hydrochloride form ( $C_{28}H_{39}NO_6 \cdot HCl$ ); rimexolone ((11 $\beta$ ,16 $\alpha$ ,17 $\beta$ )-11-hydroxy-16,17-dimethyl-17-(1-oxopropyl)androsta-1,4-dien-3-one); rofleponide ((2R)-6 $\alpha$ ,9 $\alpha$ -Difluoro-11 $\beta$ ,21-dihydroxy-16 $\alpha$ ,17 $\alpha$ -propylmethylenedioxy-pregn-4-ene-3,20-dione); tipredane ((11 $\beta$ , 17 $\alpha$ )-17-(ethylthio)-9 $\alpha$ -fluoro-11 $\beta$ -hydroxy-17-(methylthio) androsta-1,4-dien-3-one); tixocortol ((11 $\beta$ )-11,17-dihydroxy-21-mercaptopregn-4-ene-3,20-dione), or its 21-pivalate form ( $C_{26}H_{38}O_5S$ ; (11 $\beta$ )-21-[(2,2-dimethyl-1-oxopropyl)thio]-11,17-dihydroxypregn-4-ene-3,20-dione); triamcinolone ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11,16,17,21-tetrahydroxypregna-1,4-diene-3,20-dione), or its 16,21-diacetate form ( $C_{25}H_{31}FO_8$ ; (11 $\beta$ ,16 $\alpha$ )-16,21-bis(acetyloxy)-9-fluoro-11,17-dihydroxypregna-1,4-diene-3,20-dione); Triamcinolone acetone ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11,21-dihydroxy-16,17-[1-methylethylidenebis(oxy)]pregna-1,4-diene-3,20-dione), its 21-acetate crystal form, its 21-disodium phosphate form ( $C_{24}H_{30}FNa_2O_9P$ ), or its 21-hemisuccinate form ( $C_{28}H_{35}FO_9$ ); triamcinolone benetonide ((11 $\beta$ ,16 $\alpha$ )-21-[3-(benzoylamino)-2-methyl-1-oxopropoxy]-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); or triamcinolone hexacetone; ((11 $\beta$ ,16 $\alpha$ )-21-(3,3-dimethyl-1-oxobutoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione), analogues thereof, or pharmaceutically or veterinarily acceptable salts thereof.

35. The composition of claim 1, wherein the second agent comprises a glucocorticoid steroid selected from budesonide, testosterone, progesterone, estrogen, flunisolide, triamcinolone, beclomethasone, betamethasone, dexamethasone, fluticasone, methylprednisolone, prednisone, hydrocortisone, or mometasone.

36. The composition of claim 1, wherein the first active agent comprises a single stranded anti-sense DNA oligo.

37. The composition of claim 1, wherein the first active agent comprise(s) a double stranded DNA oligo.

38. The composition of claim 1, wherein the first active agent comprises a single stranded anti-sense RNA oligo(s).

39. The composition of claim 1, wherein the first active agent comprises a double stranded RNA oligo(s).

40. The composition of claim 1, which is a systemic or topical formulation.

41. The formulation of claim 40, selected from oral, intrabuccal, intrapulmonary, rectal, intrauterine, intratumor, intracranial, nasal, intramuscular, subcutaneous, intravascular, intrathecal, inhalable, transdermal, intradermal, intracavitary, implantable, iontophoretic, ocular, vaginal, intraarticular, otical, intravenous, intramuscular, intraglandular, intraorgan, intralymphatic, implantable, slow release or enteric coating formulations.

42. The formulation of claim 41, which is an oral formulation, wherein the carrier is selected from solid or liquid carriers.

43. The formulation of claim 42, in the form of a powder, dragees, tablets, capsules, sprays, aerosols, solutions, suspensions and emulsions, or optionally oil-in-water or water-in-oil emulsions.

44. The formulation of claim 41, which is a topical formulation, in the form of cream, gel, ointment, spray, aerosol, patch, solution, suspension or emulsion.

45. The formulation of claim 41, which is an injectable formulation, in the form of an aqueous or alcoholic solution or suspension, an oily solution or suspension, or an oil-in-water or water-in-oil emulsion.

46. The formulation of claim 41, in the form of a rectal or vaginal formulation, optionally a suppository.

47. The formulation of claim 41, in the form of a transdermal formulation, wherein the carrier comprises an aqueous or alcoholic solution, an oily solution or suspension, or an oil-in-water or water-in-oil emulsion.

48. The formulation of claim 47, in the form of an iontophoretic transdermal formulation, wherein the carrier comprises an aqueous or alcoholic solution, an oily solution or suspension, or an oil-in-water or water-in-oil emulsion, and wherein the formulation further comprises a transdermal transport promoting agent.

49. The formulation of claim 41, in the form of an implant, a capsule, a cartridge or a blister.

50. The formulation of claim 49, in the form of an aqueous or alcoholic solution or suspension, an oily solution or suspension, or an oil-in-water or water-in-oil emulsion.

51. The formulation of claim 40, wherein the carrier comprises a hydrophobic carrier.

52. The formulation of claim 51, wherein the carrier comprises lipid vesicles, optionally liposomes; or particles, optionally microcrystals.
53. The formulation of claim 52, wherein the carrier comprises liposomes, and the liposomes comprise the active agent(s).
54. The formulation of claim 41, which is a respirable or inhalable formulation, optionally aerosolizable or sprayable of particle size about 0.05 to about 10 micron.
55. The formulation of claim 54, having a particle size about 0.1 to about 5 micron.
56. The formulation of claim 41, which is a nasal or intrapulmonary formulation, optionally aerosolizable or sprayable of particle size about 8 to about 200 micron.
57. The formulation of claim 56, of particle size about 10 to about 50 micron.
58. The formulation of claim 41, in single or multiple unit form.
59. The formulation of claim 41, in bulk.
60. A therapeutic or prophylactic kit, comprising a delivery device; in separate containers, the active agent(s) of claim 1; and instructions for adding a carrier and preparing a formulation and for use of the kit.
61. The kit of claim 60, wherein the device delivers single metered doses of the formulation.
62. The kit of claim 60, wherein the formulation is a respirable formulation, and the delivery device comprises a nebulizer or a dry powder inhaler.
63. The kit of claim 62, wherein the device comprises a nebulizer or an insufflator and the formulation is provided in a pierceable or openable capsule or cartridge.
64. The kit of claim 60, wherein the delivery device comprises a pressurized inhaler and the agent(s) is (are) provided as a suspension, solution or dry formulation of the active agent(s).
65. The kit of claim 60, further comprising, in a separate container, an agent selected from other therapeutic agents, surfactants, anti-oxidants, flavoring agents, fillers, volatile oils, dispersants, antioxidants, propellants, preservatives, buffering agents, RNA inactivating agents, cell-internalized or up-taken agents or coloring agents.
66. The kit of claim 60, comprising, in separate containers, one or more oligos, one or more AIS of formula (Ia), or (Ib) one or more surfactants, a carrier or diluent, optionally other therapeutic agents, and instructions for scheduling the administration of first and second agents.
67. The kit of claim 66, further comprising one or more ubiquinone(s), and instructions for scheduling the administration of first and second agents.
68. The kit of claim 60, wherein the device is a transdermal delivery device, and the kit further comprises a transdermal delivery agent, a transdermal carrier or diluent, and instructions for preparing and delivering a transdermal delivery formulation.
69. The kit of claim 60, wherein the device is an iontophoretic delivery device, and the kit further comprises an iontophoretic agent(s) and instructions for preparing and delivering an iontophoretic formulation.
70. The kit of claim 60, comprising, in separate containers, one or more oligo(s), one or more ubiquinone(s), one or more surfactants, a carrier or diluent, optionally other therapeutic agents, and instructions for scheduling the administration of first and second agents.
71. A method of preventing or treating a respiratory, lung or malignant disease or condition, comprising simultaneously, sequentially or separately administering to a subject in need of treatment, preventative, prophylactic or therapeutic amounts of the first and second active agents of claim 1.
72. The method of claim 71, wherein the oligo(s) and the AIS are administered in amounts effective for alleviating bronchoconstriction and/or lung inflammation or allergy(ies) and/or surfactant depletion or hyposecretion.
73. The method of claim 71, wherein the oligo(s) and the ubiquinone(s) are administered in amounts effective for alleviating bronchoconstriction, lung inflammation or allergies, or ubiquinone or lung surfactant depletion.
74. The method of claim 71, wherein one or more of the agent(s) is (are) administered as a nasal, inhalable, respirable or intrapulmonary composition(s) into the subject's respiratory system.
75. The method of claim 74, wherein one or more of the agents are administered intrapulmonarily or by inhalation.
76. The method of claim 74, wherein the respirable or inhalable composition(s) comprise(s) particles

about 0.05 to about 10 micron in size.

77. The method of claim 74, wherein the nasal or intrapulmonary composition comprises particles about 8 to about 100 micron in diameter.

78. The method of claim 74, wherein the composition(s) is (are) administered as a respirable aerosol.

79. The method of claim 71, wherein the ubiquinone(s) is (are) administered orally, and the oligo(s) and the AIS are administered through the respiratory tract.

80. The method of claim 71, wherein the disease or condition is associated with pulmonary obstruction, bronchoconstriction, lung inflammation or allergy(ies), adenosine hypersensitivity, adenosine or adenosine receptor(s), hyperproduction, or surfactant or ubiquinone hypoproduction.

81. The method of claim 71, wherein the disease or condition comprises pulmonary vasoconstriction, respiratory inflammation or allergies, asthma, impeded respiration, respiratory distress syndrome (RDS), lung pain, cystic fibrosis (CF), allergic rhinitis (AR), apnea, pulmonary hypertension, emphysema, chronic obstructive pulmonary disease (COPD), pulmonary transplantation rejection, pulmonary fibrosis, pulmonary infections, bronchitis, or cancer.

82. The method of claim 71, wherein the disease or condition is associated with respiratory allergies, and the first active agent(s) is anti-sense to the initiation codon, the coding region, the 5'-end or the 3'-end genomic flanking regions, the 5' or 3' intron-exon junctions, or regions within 2 to 10 nucleotides of the junctions of at least one gene(s) encoding, or regulating expression of, an immunoglobulin(s), antibody(ies), or immunoglobulin or antibody receptors, or are anti-sense to the immunoglobulin(s), antibody(ies), or immunoglobulin or antibody receptor mRNA; MTAs of the oligo(s) or combinations thereof.

83. The method of claim 71, wherein the disease or condition is associated with a malignancy or cancer, and the oligo is anti-sense to the initiation codon, the coding region, the 5'-end or the 3'-end genomic flanking regions, the 5' or 3' intron-exon junctions, or regions within 2 to 10 nucleotides of the junctions of an oncogene(s) or at least one gene that regulates expression of, or encodes, a malignancy associated protein, or is(are) anti-sense to the oncogene or malignancy associated mRNA; MTAs or combinations thereof.

84. The method of claim 71, wherein the composition is administered transdermally or systemically.

85. The method of claim 71, wherein the composition is administered orally, intracavitarily, intranasally, intraurethral, intracavernous, intraanally, intravaginally, intrauterally, intraarticularly, transdermally, intrabucally, intravenously, subcutaneously, intramuscularly, intravascularly, intratumorously, intraglandularly, intraocularly, intracranial, into an organ, intravascularly, intrathecally, intralymphatically, intraotically, by implantation, by inhalation, intradermally, intrapulmonarily, intraotically, by slow release, by sustained release and by a pump.

86. The method of claim 71, wherein the mammal(s) is a human or non-human mammal.

87. The method of claim 71, wherein the oligo(s) is (are) administered in amount of about 0.005 to about 150 mg/kg body weight.

88. The method of claim 71, wherein the oligo(s) contain(s) up to about 15%A.

89. The method of claim 71, wherein the oligo(s) is (are) substantially free of A.

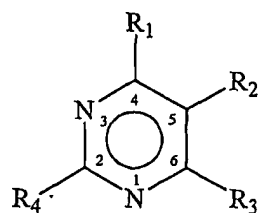
90. The method of claim 71, wherein the target comprises transcription factors, stimulating or activating factors, interleukins, interleukin receptors, chemokines, chemokine receptors, endogenously produced specific or non-specific enzymes, immunoglobulins, antibody receptors, central nervous system (CNS) or peripheral nervous or non-nervous system receptors, CNS and peripheral nervous and non-nervous system peptide transmitters, adhesion molecules, defensins, growth factors, microbial targets, vasoactive peptides, peptide receptors or binding proteins, or malignancy associated proteins.

91. The method of claim 71, wherein one or more As in the oligo(s) is(are) substituted by a universal base that comprise(s) a heteroaromatic base(s) that bind(s) to thymidine or uridine but has(have) less than about 0.3 of the adenosinebase agonist or antagonist activity at an adenosine A<sub>1</sub>, A<sub>2a</sub>, A<sub>2b</sub> or A<sub>3</sub> receptor.

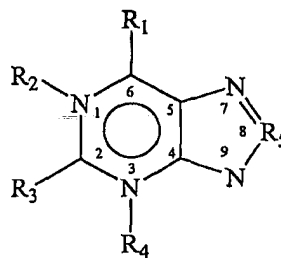
92. The method of claim 91, wherein the heteroaromatic base(s) comprise(s) pyrimidines or purines, which may be substituted by O, halo, NH<sub>2</sub>, SH, SO, SO<sub>2</sub>, SO<sub>3</sub>, COOH, branched or fused primary or secondary amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, alkoxy, alkenoxy, acyl, cycloacyl, arylacyl, alkynoxy, cycloalkoxy, aroyl, arylthio, arylsulfoxyl, halocycloalkyl, alkylcycloalkyl, alkenylcycloalkyl, alkynylcycloalkyl, haloaryl, alkylaryl, alkenylaryl, alkynylaryl, arylalkyl, arylalkenyl, arylalkynyl, arylcycloalkyl, all of which may be further substituted by O, halo, NH<sub>2</sub>, primary, secondary or tertiary amine, SH, SO, SO<sub>2</sub>, SO<sub>3</sub>,

cycloalkyl, heterocycloalkyl or heteroaryl.

93. The method of claim 91, wherein the purines are substituted at positions 1, 2, 3, 6, and/or 8, the pyrimidines are substituted at positions 2, 3, 4, 5 and/or 6 and have the chemical formula



pyrimidines



purines

or

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$  and  $R^5$  are independently H, alkyl, alkenyl or alkynyl and  $R^3$  is H, aryl, dicycloalkyl, dicycloalkenyl, dicycloalkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, O-cycloalkyl, O-cycloalkenyl, O-cycloalkynyl,  $NH_2$ -alkylamino-ketoxyalkyloxy-aryl, or mono or dialkylaminoalkyl-N-alkylamino- $SO_2$ aryl, and  $R^4$  and  $R^5$  are independently  $R^1$  and together are  $R^3$ , and the pyrimidines and purines optionally comprise theophylline, caffeine, dyphylline, etophylline, acephylline piperazine, bamifylline, enprofylline or xanthine.

94. The method of claim 93, wherein the universal base(s) comprise(s) 3-nitropyrrole-2'-deoxynucleoside, 5-nitro-indole, 2-deoxyribosyl-(5-nitroindole), 2-deoxyribofuranosyl-(5-nitroindole), 2'-deoxyinosine, 2'-deoxynebularine, 6H, 8H-3,4-dihydropyrimido [4,5-c] oxazine-7-one, or 2-amino-6-methoxyaminopurine.

95. The method of claim 71, wherein the second active agent comprises an AIS of formula (Ia) selected from dehydroepiandrosterone, 16-alpha-bromodehydroepiandrosterone, 16-alpha-fluorodehydroepiandrosterone, etiocholanolone, dehydroepiandrosterone sulfate or other pharmaceutically or veterinarily acceptable salts thereof.

96. The method of claim 71, wherein the second active agent comprises an AIS formula (Ib), wherein  $R^{15}$  and  $R^{16}$  together are  $=O$ ;  $R^5$  is  $-OH$ ;  $R^5$  is  $-OSO_2R^{20}$ ;  $R^{15}$  and  $R^{20}$  together is H; or pharmaceutically or veterinarily acceptable salts thereof.

97. The method of claim 71, wherein the active agents are present in an amount of about 0.01 to about 99.99 w/w of the composition.

98. The method of claim 71, wherein the second active agent comprises an AIS selected from 21-acetoxypregnenolone ((3 $\beta$ )-21-(acetyloxy)-3-hydroxypregn-5-en-20-one); alclometasone ((7 $\alpha$ , 11 $\beta$ , 16 $\alpha$ )-7-Chloro-11, 17, 21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), or its 17,21-dipropionate form ( $C_{28}H_{37}ClO_7$ ); algestone ((16 $\alpha$ )-16,17-dihydroxypregn-4-ene-3,20-dione), its cyclic acetal with acetone form ( $C_{24}H_{34}O_4$ ), or its 16 $\alpha$ -methyl ether form ( $C_{22}H_{32}O_4$ ); amcinonide ((11 $\beta$ , 16 $\alpha$ )-21-(acetyloxy)-16,17-[cyclopentylidenebis(oxy)]-9-fluoro-11-hydroxypregna-1,4-di-ene-3,20-dione); beclomethasone ((11 $\beta$ ,16 $\beta$ )-9-chloro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its dipropionate form ( $C_{28}H_{37}ClO_7$ ), or its monopropionate form; betamethasone ((11 $\beta$ , 16 $\beta$ )-9-fluoro-11, 17, 21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{24}H_{31}FO_6$ ), its 21-adamantoate form ( $C_{33}H_{43}FO_6$ ), its 17-benzoate form ( $C_{29}H_{33}FO_6$ ), its 17, 21-dipropionate form ( $C_{28}H_{37}FO_7$ ), its 17-valerate form ( $C_{27}H_{37}FO_6$ ), or its 21-phosphate disodium salt form ( $C_{22}H_{28}FNa_2O_8P$ ); budesonide ((11 $\beta$ , 16 $\alpha$ )-16,17-[butylidenebis(oxy)]-11, 21-dihydropregna-1,4-diene-3,20-dione); chloroprednisone ((6 $\alpha$ )-chloro-17,21-dihydroxypregna-1,4-diene-3,11,20-trione), or its 21-acetate from ( $C_{23}H_{27}ClO_6$ ); ciclesonide; clobetasol ((11 $\beta$ ,16 $\beta$ )-21-chloro-9-fluoro-11,17-dihydroxy-16-methylpregna-1,4-diene-3,20-dione), or its 17-propionate form ( $C_{25}H_{32}ClFO_5$ ); clobetasone ((16 $\beta$ )-21-chloro-9-fluoro-17-hydroxy-16-methylpregna-1,4-diene-3,11,20-trione), or its 17-butyrate form ( $C_{26}H_{32}ClFO_5$ ); clocortolone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-9-chloro-6-fluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{24}H_{30}ClFO_5$ ), or its 21-pivalate form ( $C_{27}H_{36}ClFO_5$ ); cloprednol ((11 $\beta$ )-6-chloro-11,17,21-trihydroxypregna-1,4,6-triene-3,20-dione); coroxon

(phosphoric acid 3-chloro-4-methyl-2-oxo-2H-1-benzopyran-7-yl diethyl ester); cortisone (17,21-dihydroxypregn-4-ene-3,11,20-trione), its 21-acetate form ( $C_{23}H_{30}O_6$ ), or its 21-cyclopentanepropionate form ( $C_{29}H_{40}O_6$ ); cortivazol ((11 $\beta$ ,16 $\alpha$ )-21-(acetyloxy)-11,17-dihydroxy-6,16-dimethyl-2'-phenyl-2'H-pregna-2,4,6-trieno[3,2-c]pyrazol-20-one); deflazacort ((11 $\beta$ ,16 $\beta$ )-21-(acetyloxy)-11-hydroxy-2'-methyl-5'H-pregna-1,4-dieno[17,16-d]oxazole-3,20-dione); desonide ((11 $\beta$ ,16 $\alpha$ )-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); desoximetasone ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11, 21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione); dexamethasone ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{24}H_{31}FO_6$ ), its 21-(3,3-dimethylbutyrate) form ( $C_{28}H_{39}FO_6$ ; Chimerda et al., US Patent No. 2,939,873), its 21-diethylaminoacetate form ( $C_{28}H_{41}FNO_6$ ), its 21-isonicotinate form ( $C_{28}H_{41}FNO_6$ ), its 17,21-dipropionate form ( $C_{28}H_{37}FNO_6$ ), or its 21-palmitate form ( $C_{38}H_{59}FO_6$ ); diflorasone ((6 $\alpha$ ,11 $\beta$ ,16 $\beta$ )-6,9-difluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), or its diacetate form ( $C_{26}H_{32}F_2O_7$ ); diflucortolone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6,9-difluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione), or its 21-valerate form ( $C_{27}H_{36}F_2O_5$ ); difluprednate ((6 $\alpha$ ,11 $\beta$ )-21-(acetyloxy)-6,9-difluoro-11-hydroxy-17-(1-oxobutoxy)pregna-1,4-diene-3,20-dione); enoxolone ((3 $\beta$ ,20 $\beta$ )-3-hydroxy-11-oxoolean-12-en-29-oic acid), or its 18 $\alpha$ -hydrogen form; fluazacort ((11 $\beta$ ,16 $\beta$ )-21-(acetyloxy)-9-fluoro-11-hydroxy-2'-methyl-5'H-pregna-1,4-dieno[17,16-d]oxazole-3,20-dione); flucoronide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-9,11-dichloro-6-fluoro-21-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); flumetasone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6,9-difluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{24}H_{30}F_2O_6$ ), or its 21-pivalate form ( $C_{27}H_{36}F_2O_6$ ); flunisolide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene) bis(oxy)]pregna-1,4-diene-3,20-dione), or its 21-acetate form ( $C_{26}H_{33}FO_7$ ); fluocinolone acetate ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6,9-difluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); fluocinonide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-21-(acetyloxy)-6,9-difluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); fluocortin butyl ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11-hydroxy-16-methyl-3,20-dioxopregna-1,4-dien-21-oic acid butyl ester); fluocortolone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,21-dihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{24}H_{31}FO_5$ ), its 21-hexanoate form ( $C_{28}H_{39}FO_5$ ), or its 21-pivalate form ( $C_{22}H_{37}FO_5$ ); fluorometholone ((6 $\alpha$ ,11 $\beta$ )-9-fluoro-11,17-dihydroxy-6-methylpregna-1,4-diene-3,20-dione), or its 17-acetate form ( $C_{24}H_{31}FO_5$ ); fluperolone acetate ([11 $\beta$ ,17 $\alpha$ ,17(S)]-17-[2-(acetyloxy)-1-oxopropyl]-9-fluoro-11,17-dihydroxyandrosta-1,4-dien-3-one); fluprednidene acetate ((11 $\beta$ )-21-(acetyloxy)-9-fluoro-11,17-dihydroxy-16-methylenepregna-1,4-diene-3,20-dione); fluprednisolone ((6 $\alpha$ ,11 $\beta$ )-6-fluoro-11,17,21-trihydroxypregna-1,4-diene-3,20-dione), or its 21-acetate form ( $C_{23}H_{29}FO_6$ ); flurandrenolide ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregn-4-ene-3,20-dione); fluticasone propionate ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ ,17 $\alpha$ )-6,9-difluoro-11-hydroxy-16-methyl-3-oxo-17-(1-oxopropoxy)androsta-1,4-diene-17-carbothioic acid S-(fluoromethyl) ester); formocortal ((11 $\beta$ ,16 $\alpha$ )-21-(acetyloxy)-3-(2-chloroethoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]-20-oxopregna-3,5-diene-6-carboxaldehyde); halcinonide ((11 $\beta$ ,16 $\alpha$ )-21-chloro-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregn-4-ene-3,20-dione); halobetasol propionate ((6 $\alpha$ ,11 $\beta$ ,16 $\beta$ )-21-chloro-6,9-difluoro-11-hydroxy-16-methyl-17-(1-oxopropoxy)pregna-1,4-diene-3,20-dione); halometasone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-2-chloro-6,9-difluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), or its monohydrate form ( $C_{22}H_{27}ClF_2O_5 \cdot H_2O$ ); halopredone acetate ((6 $\beta$ ,11 $\beta$ )-17,21-bis(acetyloxy)-2-bromo-6,9-difluoro-11-hydroxypregna-1,4-diene-3,20-dione); hydrocortamate (N,N-diethylglycine (11 $\beta$ )-11,17-dihydroxy-3,20-dioxopregn-4-en-21-yl ester), or its hydrochloride form ( $C_{27}H_{41}NO_6 \cdot HCl$ ); hydrocortisone ((11 $\beta$ )-11,17,21-trihydroxypregn-4-ene-3,20-dione), its 21-acetate form ( $C_{23}H_{32}O_6$ ), its 17-butyrate form ( $C_{25}H_{36}O_6$ ), its 21-phosphate disodium salt form ( $C_{21}H_{29}Na_2O_8P$ ), its 21-sodium succinate form ( $C_{25}H_{33}NaO_8$ ), its 17-valerate form ( $C_{26}H_{38}O_6$ ), or its cypionate form; loteprednol etabonate ((11 $\beta$ ,17 $\alpha$ )-17-[(ethoxycarbonyl)oxy]-11-hydroxy-3-oxoandrosta-1,4-diene-17-carboxylic acid chloromethyl ester); mazipredone ((11 $\beta$ )-11,17-dihydroxy-21-(4-methyl-1-piperazinyl)pregna-1,4-diene-3,20-dione), or its hydrochloride form ( $C_{26}H_{38}N_2O_4 \cdot HCl$ ); medrysone ((6 $\alpha$ ,11 $\beta$ )-11-hydroxy-6-methylpregn-4-ene-3,20-dione); meprednisone ((16 $\beta$ )-17,21-dihydroxy-16-methylpregna-1,4-diene-3,11,20-trione), or its 21-acetate form ( $C_{24}H_{30}O_6$ ); methylprednisolone ((6 $\alpha$ ,11 $\beta$ )-11,17,21-trihydroxy-6-methylpregna-1,4-diene-3,20-dione; Sebek and Spero, US Patent No. 2,897,218, and Gould, US Patent No. 3,053,832), its 21-acetate form ( $C_{24}H_{32}O_6$ ), its 21-phosphate disodium salt form ( $C_{22}H_{29}Na_2O_8P$ ), its 21-succinate sodium salt form ( $C_{26}H_{33}NaO_8$ ), or its aceponate form ( $C_{27}H_{36}O_7$ ); mometasone furoate ((11 $\beta$ ,16 $\alpha$ )-9,21-dichloro-17-[(2-furanylcarbonyl)oxy]-11-hydroxy-16-methylpregna-1,4-diene-3,20-dione); paramethasone ((6 $\alpha$ ,11 $\beta$ ,16 $\alpha$ )-6-

fluoro-11,17,21-trihydroxy-16-methylpregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{24}H_{31}FO_6$ ), its disodium phosphate form, or a mixture of its 21-acetate and disodium phosphate form; prednicarbate ((11 $\beta$ )-17[(ethoxycarbonyl)oxy]-11-hydroxy-21-(1-oxopropoxy)pregna-1,4-diene-3,20-dione); prednisolone ((11 $\beta$ )-11,17,21-trihydroxypregna-1,4-diene-3,20-dione), its 21-acetate form ( $C_{23}H_{30}O_6$ ), its 21-*tert*-butylacetate form ( $C_{27}H_{38}O_6$ ; Sarrett), its 21-hydrogen succinate form ( $C_{25}H_{32}O_8$ ), its 21-succinate sodium salt form ( $C_{25}H_{31}NaO_8$ ), its 21-stearoylglycolate form ( $C_{41}H_{64}O_8$ ), its 21-*m*-sulfobenzoate sodium salt form ( $C_{28}H_{31}NaO_9S$ ; (11 $\beta$ )-11,17-dihydroxy-21-[(3-sulfobenzoyl)oxy]pregna-1,4-diene-3,20-dione monosodium salt), or its 21-trimethylacetate form ( $C_{26}H_{36}O_6$ ); prednisolone 21-diethylaminoacetate (N,N-diethylglycine (11 $\beta$ )-11,17-dihydroxy-3,20-dioxopregna-1,4-dien-21-yl ester; British Patent No. 862,370), or its hydrochloride form ( $C_{27}H_{39}NO_6 \cdot HCl$ ); prednisolone sodium phosphate (11,17-dihydroxy-21-(phosphonoxy)pregna-1,4-diene-3,20-dione disodium salt); prednisone (17,21-dihydroxypregna-1,4-diene-3,11,20-trione), or its 21-acetate form ( $C_{23}H_{28}O_6$ ); prednival ((11 $\beta$ )-11,21-dihydroxy-17-[(1-oxopentyl)oxy]pregna-1,4-diene-3,20-dione), or its 21-acetate form ( $C_{28}H_{38}O_7$ ); prednylidene ((11 $\beta$ )-11,17,21-trihydroxy-16-methylenepregna-1,4-diene-3,20-dione), or its 21-diethylaminoacetate hydrochloride form ( $C_{28}H_{39}NO_6 \cdot HCl$ ); rimexolone ((11 $\beta$ ,16 $\alpha$ ,17 $\beta$ )-11-hydroxy-16,17-dimethyl-17-(1-oxopropyl)androsta-1,4-dien-3-one); rofleponide ((22R)-6 $\alpha$ ,9 $\alpha$ -Difluoro-11 $\beta$ ,21-dihydroxy-16 $\alpha$ ,17 $\alpha$ -propylmethylenedioxypregn-4-ene-3,20-dione); tipredane ((11 $\beta$ , 17 $\alpha$ )-17-(ethylthio)-9 $\alpha$ -fluoro-11 $\beta$ -hydroxy-17-(methylthio) androsta-1,4-dien-3-one); tixocortol ((11 $\beta$ )-11,17-dihydroxy-21-mercaptopregn-4-ene-3,20-dione), or its 21-pivalate form ( $C_{26}H_{38}O_5S$ ; (11 $\beta$ )-21-[(2,2-dimethyl-1-oxopropyl)thio]-11,17-dihydroxypregn-4-ene-3,20-dione); triamcinolone ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11,16,17,21-tetrahydroxypregna-1,4-diene-3,20-dione), or its 16,21-diacetate form ( $C_{25}H_{31}FO_8$ ; (11 $\beta$ ,16 $\alpha$ )-16,21-bis(acetyloxy)-9-fluoro-11,17-dihydroxypregna-1,4-diene-3,20-dione); Triamcinolone acetonide ((11 $\beta$ ,16 $\alpha$ )-9-fluoro-11,21-dihydroxy-16,17-[1-methylethylidenebis(oxy)]pregna-1,4-diene-3,20-dione), its 21-acetate crystal form, its 21-disodium phosphate form ( $C_{24}H_{30}FNa_2O_9P$ ), or its 21-hemisuccinate form ( $C_{28}H_{35}FO_9$ ); triamcinolone benetonide ((11 $\beta$ ,16 $\alpha$ )-21-[3-(benzoylamino)-2-methyl-1-oxopropoxy]-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene)bis(oxy)]pregna-1,4-diene-3,20-dione); or triamcinolone hexacetone; ((11 $\beta$ ,16 $\alpha$ )-21-(3,3-dimethyl-1-oxobutoxy)-9-fluoro-11-hydroxy-16,17-[(1-methylethylidene) bis(oxy)]pregna-1,4-diene-3,20-dione), or pharmaceutically or veterinarily acceptable salts thereof.

99. The method of claim 71, wherein the second active agent comprises an AIS selected from budesonide, testosterone, progesterone, estrogen, flunisolide, triamcinolone, beclomethasone, betamethasone, dexamethasone, fluticasone, methylprednisolone, prednisone, hydrocortisone, or mometasone.

100. A method of enhancing the prophylactic or therapeutic respiratory effect of an anti-inflammatory steroid in a subject, comprising administering to the subject, in addition to the AIS, the oligonucleotide(s) (oligo(s)) of claim 1, the AIS and the oligo(s) being administered in amounts effective for reducing or depleting levels of, or reducing sensitivity to, adenosine, reducing levels of adenosine receptors, producing bronchodilation, increasing levels of ubiquinone or lung surfactant in a subject's tissue (s), or treating bronchoconstriction, lung inflammation or lung allergies or a respiratory or lung disease or condition.

101. The method of claim 100, further administering to the subject a ubiquinone of the chemical formula.

102. The method of claim 100, wherein the steroid comprises budesonide, testosterone, progesterone, estrogen, flunisolide, triamcinolone, beclomethasone, betamethasone, dexamethasone, fluticasone, methylprednisolone, prednisone, hydrocortisone, or mometasone

103. The method of claim 100, wherein the oligo(s) is anti-sense to the initiation codon, the coding region, the 5'-end or the 3'-end genomic flanking regions, the 5' or 3' intron-exon junctions, and regions within 2 to 10 nucleotides of the junctions of at least one oncogene(s) and a gene(s) encoding or regulating expression of a target polypeptide(s) associated with lung airway dysfunction, or anti-sense to the corresponding mRNA and the polypeptide mRNA; combinations, MTAs or mixtures of the oligos; the polypeptides comprising peptide factors and transmitters, antibodies, cytokines or chemokines, enzymes, binding proteins, adhesion molecules, their receptors, or malignancy associated proteins.

104. The method of claim 100, further comprising administering to the subject other therapeutic or bioactive agents selected from analgesics, pre-menstrual medications, menopausal agents, anti-aging agents, anti-anxiety agents, mood disorder agents, anti-depressants, anti-bipolar mood agents, anti-schizophrenic agents, anti-cancer agents, alkaloids, blood pressure controlling agents, muscle relaxants, steroids, soporific agents, anti-

ischemic agents, anti-arrhythmic agents, contraceptives, vitamins, minerals, tranquilizers, neurotransmitter regulating agents, wound healing agents, anti-angiogenic agents, cytokines, growth factors, B-adrenergic receptor agonists, anti-metastatic agents, antacids, anti-histaminic agents, anti-bacterial agents, anti-viral agents, anti-gas agents, appetite suppressants, sun screens, emollients, skin temperature lowering products, radioactive phosphorescent or fluorescent contrast diagnostic or imaging agents, libido altering agents, bile acids, laxatives, anti-diarrheic agents, skin renewal agents, hair growth agents, analgesics, pre-menstrual medications, anti-menopausal agents, hormones, anti-aging agents, anti-anxiolytic agents, nociceptive agents, mood disorder agents, anti-depressants, anti-bipolar mood agents, anti-schizophrenic agents, anti-cancer agents, alkaloids, blood pressure controlling agents, other hormones, other anti-inflammatory agents, agents for treating arthritis, burns, wounds, chronic bronchitis, chronic obstructive pulmonary disease (COPD), inflammatory bowel disease such as Crohn's disease, ulcerative colitis, autoimmune disease, or lupus erythematosus, muscle relaxants, soporific agents, anti-ischemic agents, anti-arrhythmic agents, contraceptives, vitamins, minerals, tranquilizers, neurotransmitter regulating agents, wound and burn healing agents, anti-angiogenic agents, cytokines, growth factors, anti-metastatic agents, antacids, anti-histaminic agents, anti-bacterial agents, anti-viral agents, anti-gas agents, agents for reperfusion injury, counteracting appetite suppressants, sun screens, emollients, skin temperature lowering products, radioactive phosphorescent or fluorescent contrast diagnostic or imaging agents, libido altering agents, bile acids, laxatives, anti-diarrheic agents or skin renewal agents.

105. The method of claim 100, wherein the oligo(s) and/or the steroid(s) is(are) administered with surfactant protein A, surfactant protein B, surfactant protein C, surfactant protein D and surfactant Protein E, disaturated phosphatidyl choline (other than dipalmitoyl), dipalmitoyl phosphatidyl choline, phosphatidyl choline, phosphatidyl glycerol, phosphatidyl inositol, phosphatidyl ethanolamine, phosphatidyl serine; phosphatidic acid, ubiquinones, lysophosphatidyl ethanolamine, lysophosphatidyl choline, palmitoyl- lysophosphatidyl choline, dehydroepiandrosterone, dolichols, sulfatidic acid, glycerol-3-phosphate, dihydroxyacetone phosphate, glycerol, glycerol-3-phosphocholine, dihydroxy acetone, palmitate, cytidine diphosphate (CDP) diacyl glycerol, CDP choline, choline, choline phosphate; natural or artificial lamellar bodies as carrier surfactant vehicles, omega-3 fatty acids, polyenic acid, polyenoic acid, lecithin, palmitinic acid, non-ionic block copolymers of ethylene or propylene oxides, polyoxypropylene, monomeric or polymeric, polyoxyethylene, monomeric and polymeric, poly (vinyl amine) with dextran and/or alkanoyl side chains, Brij 35, Triton X-100 or synthetic surfactants ALEC, Exosurf, Survan or Atovaquone.

106. The method of claim 100, wherein the AIS comprises a steroid of chemical formula (Ia) or (Ib).

107. The method of claim 106, wherein the AIS is selected from budesonide, testosterone, progesterone, fluticasone, beclomethasone, prednisone, mometasone, estrogen, dexamethasone, hydrocortisone, triamcinolone, flunisolide, methylprednisolone prednisone, hydrocortisone, or analogues thereof.

108. The method of claim 100, wherein the first and second active agents are administered systemically or topically.

109. The method of claim 100, wherein the first and second active agents are administered as an oral, intrabuccal, intrapulmonary, rectal, intrauterine, intratumor, intracranial, nasal, intramuscular, subcutaneous, intravascular, intrathecal, inhalable, transdermal, intradermal, intracavitary, implantable, iontophoretic, ocular, vaginal, intraarticular, otical, intravenous, intramuscular, intraglandular, intraorgan, intralymphatic, implantable, slow release or enteric coating formulation.

110. The method of claim 101, wherein the ubiquinone is administered orally.

107. The method of claim 106, wherein the oligo(s) and the AIS is(are) administered intrapulmonarily, into the respiration, nasally, or by inhalation.

108. The method of claim 106, wherein the oligo(s) or the AIS is(are) administered as a respirable or inhalable formulation, optionally an aerosol of particle size about 0.05 to about 10 micron.

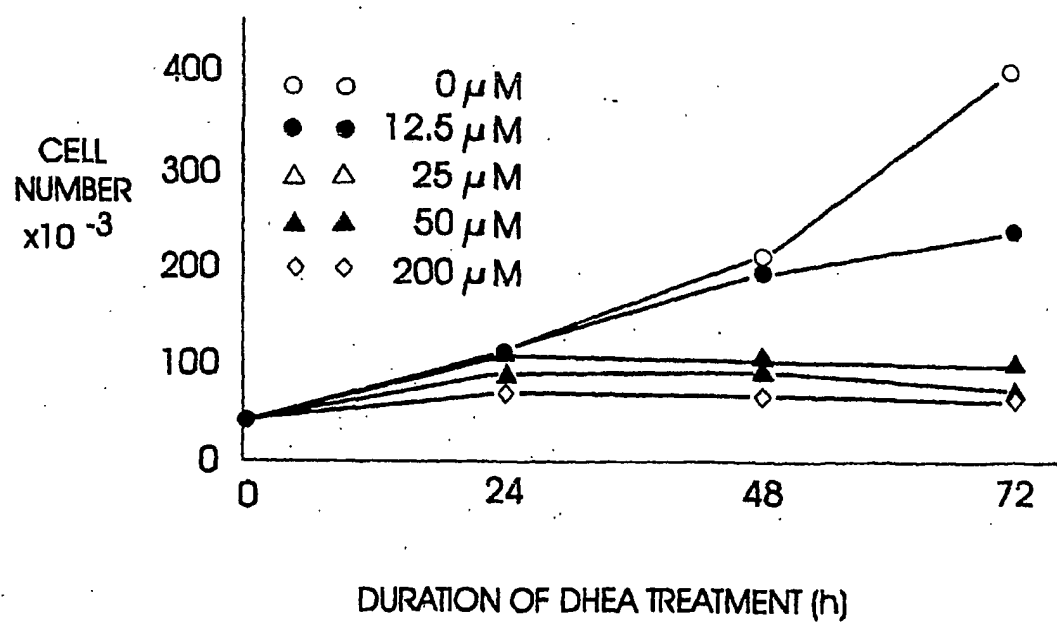
109. The method of claim 107, wherein the formulation comprises an oligo(s) or AIS of particle size about 0.1 micron to about 5 micron.

110. The method of claim 106, wherein the oligo(s) or the AIS is(are) administered nasally or intrapulmonarily, optionally an aerosol of particle size about 8 to about 100 micron.

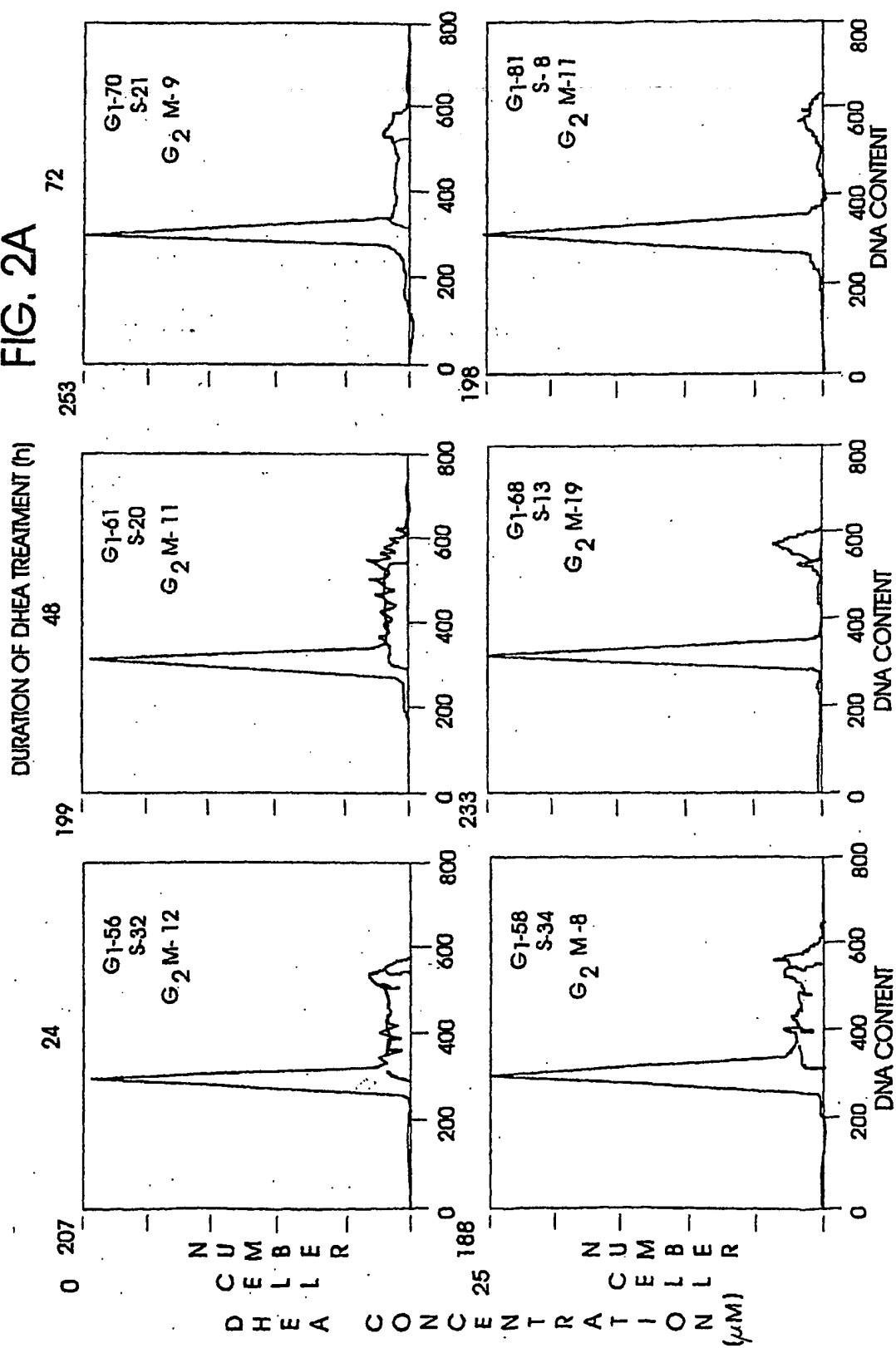
111. The method of claim 109, wherein the oligo(s) or the AIS has(have) a particle size about 10 to about 50 micron.

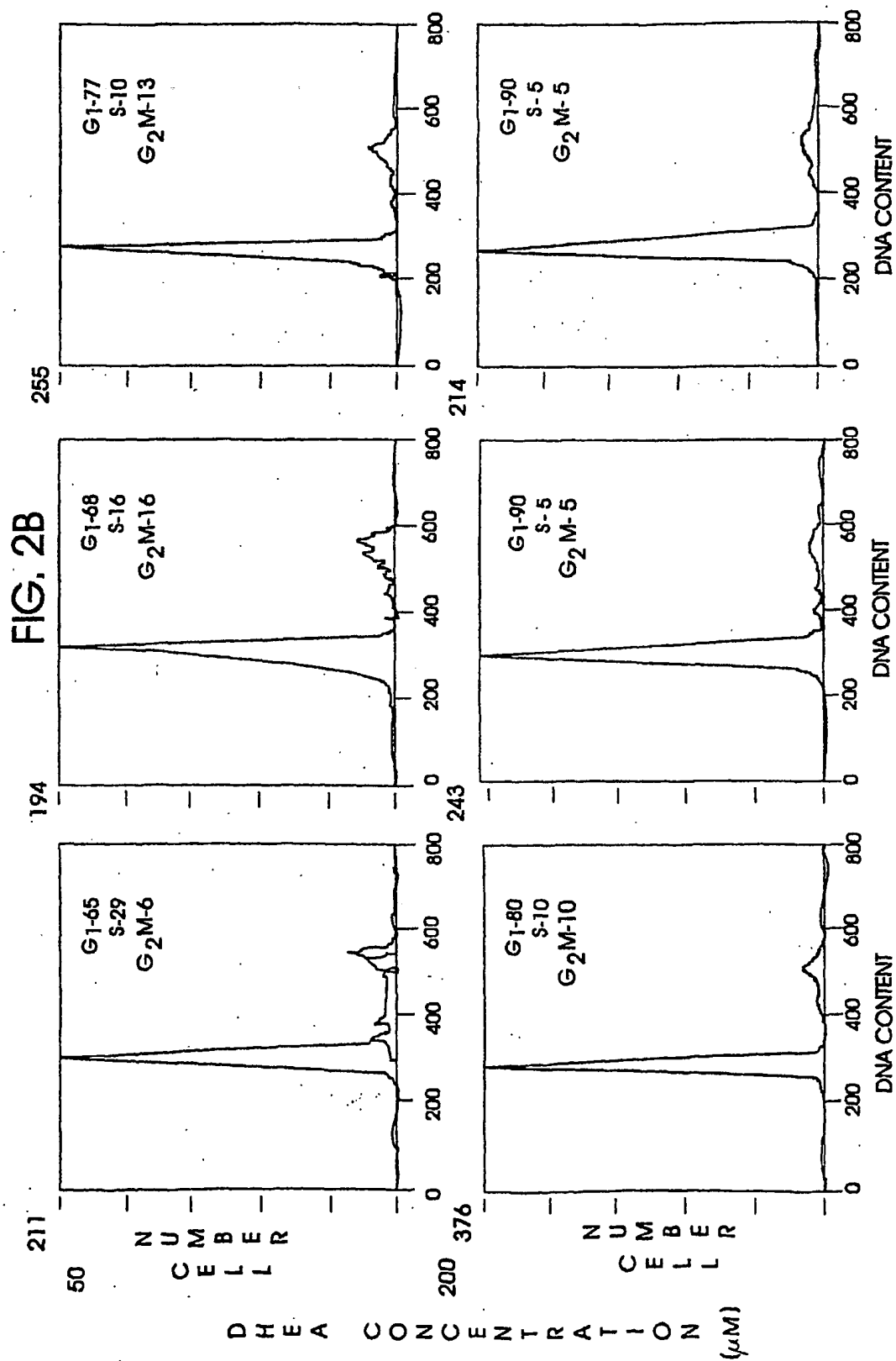


FIG. 1



**FIG. 2A**





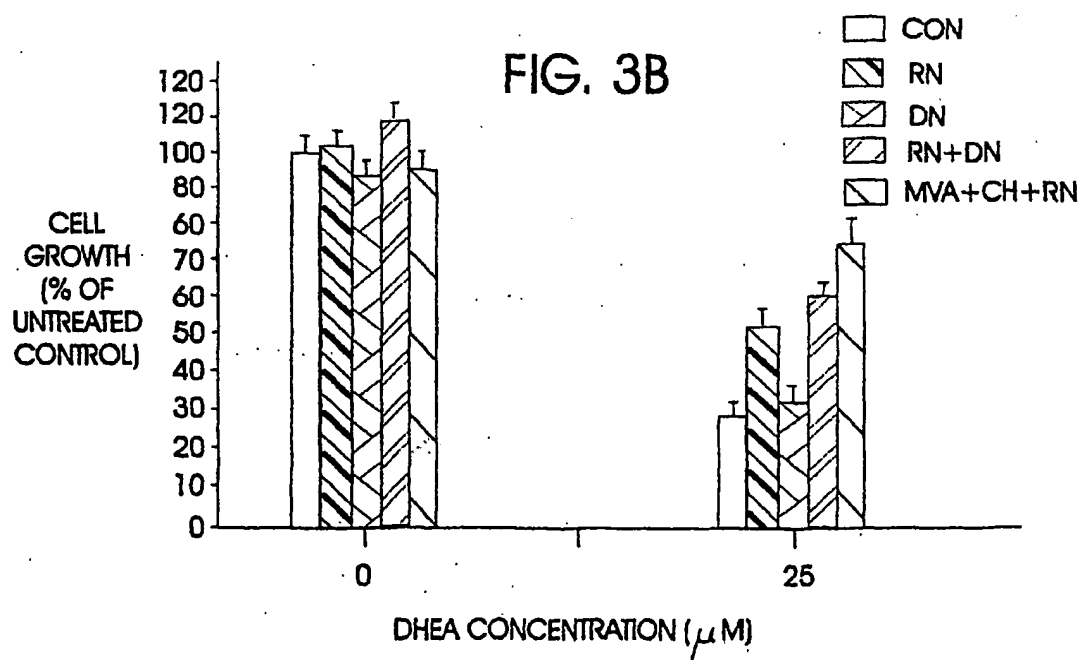
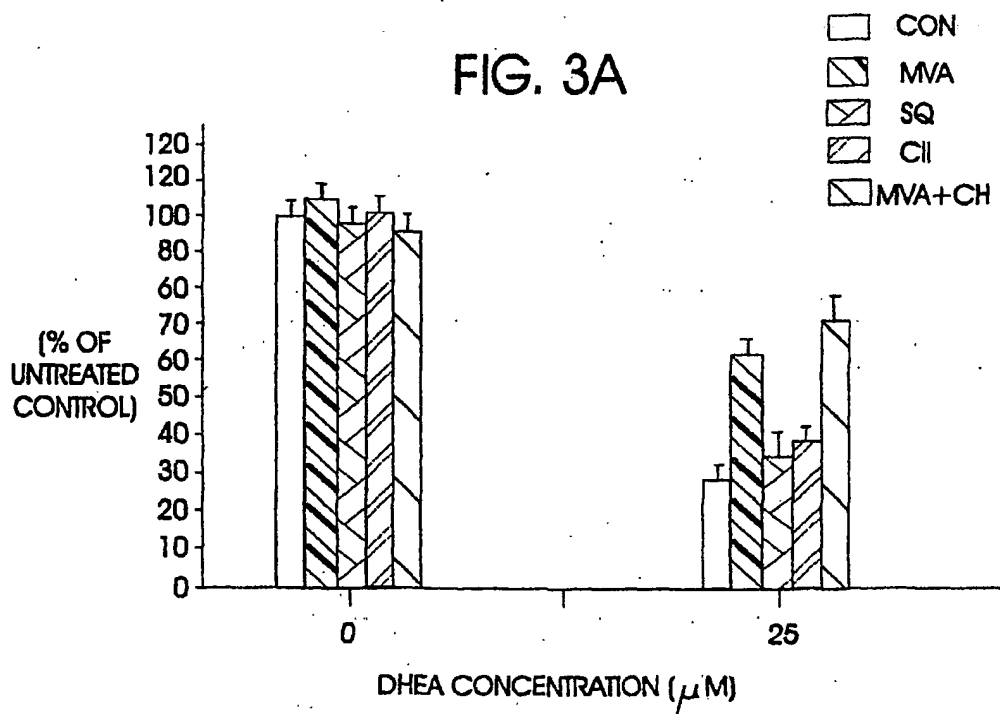


FIG. 4A

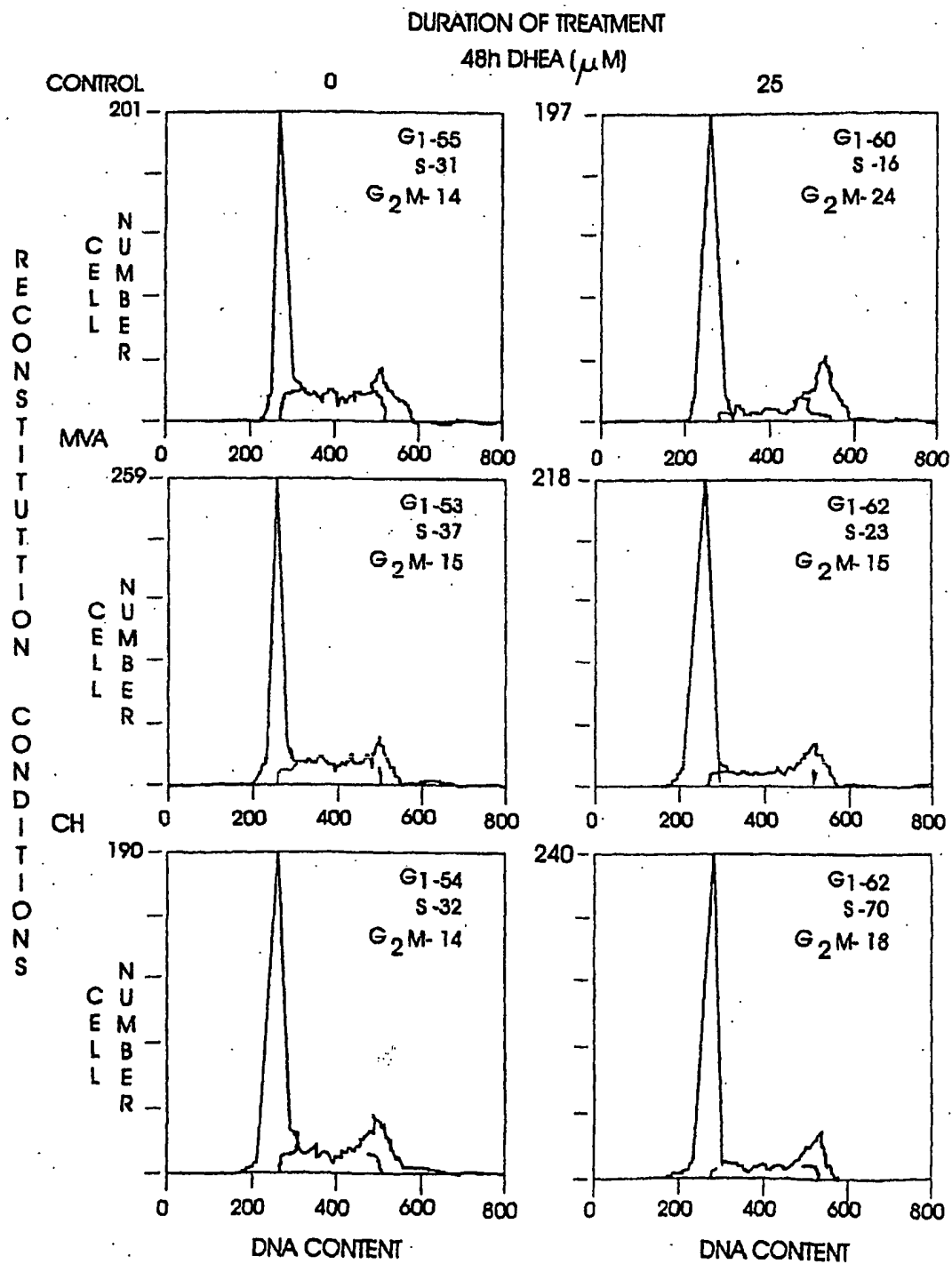


FIG. 4B

### DURATION OF TREATMENT

72h DHEA ( $\mu$ M)

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# RECONSTITUTION CONDITIONS

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**MVA**

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## DNA CONTENT

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283

## DNA CONTENT

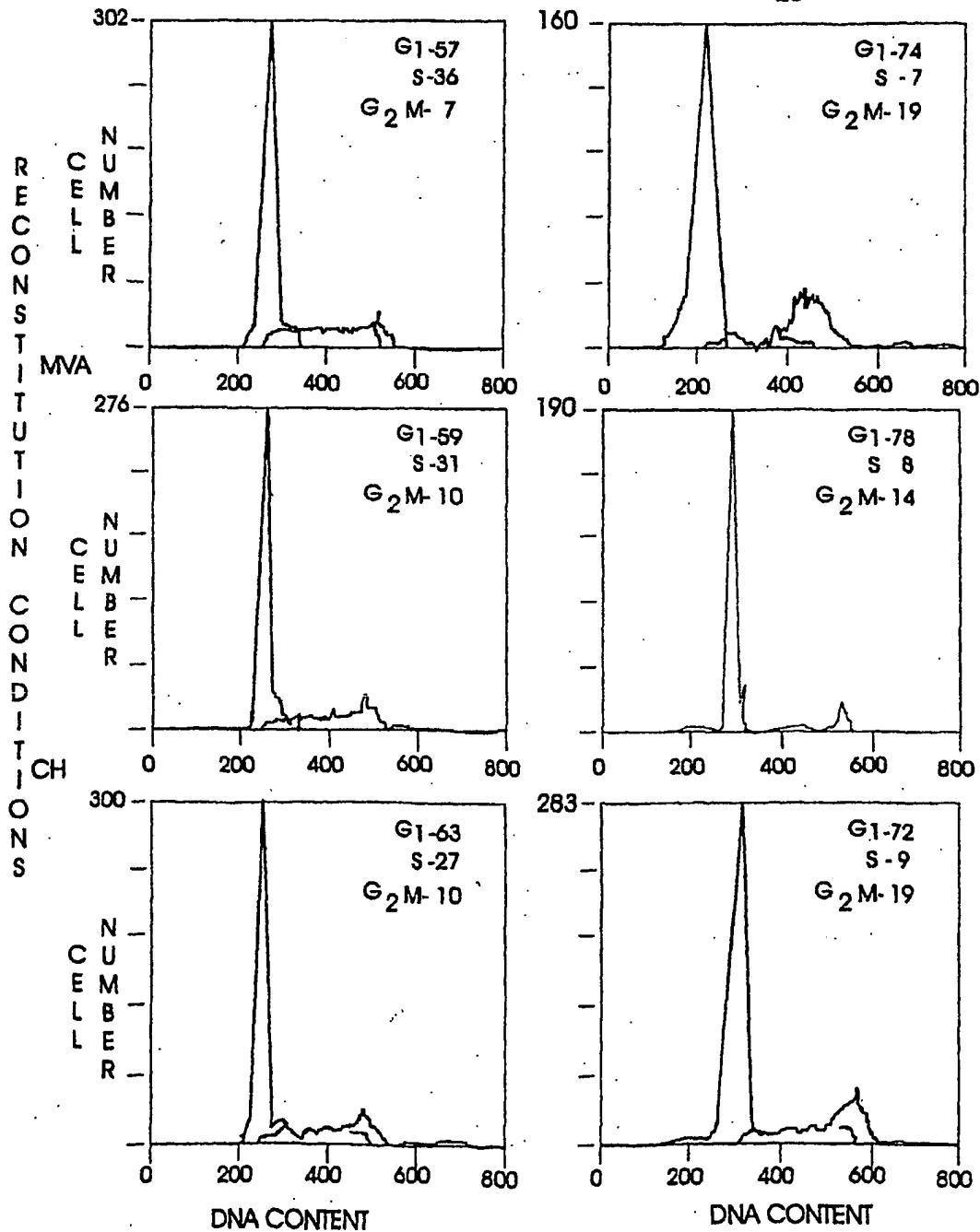


FIG. 4C

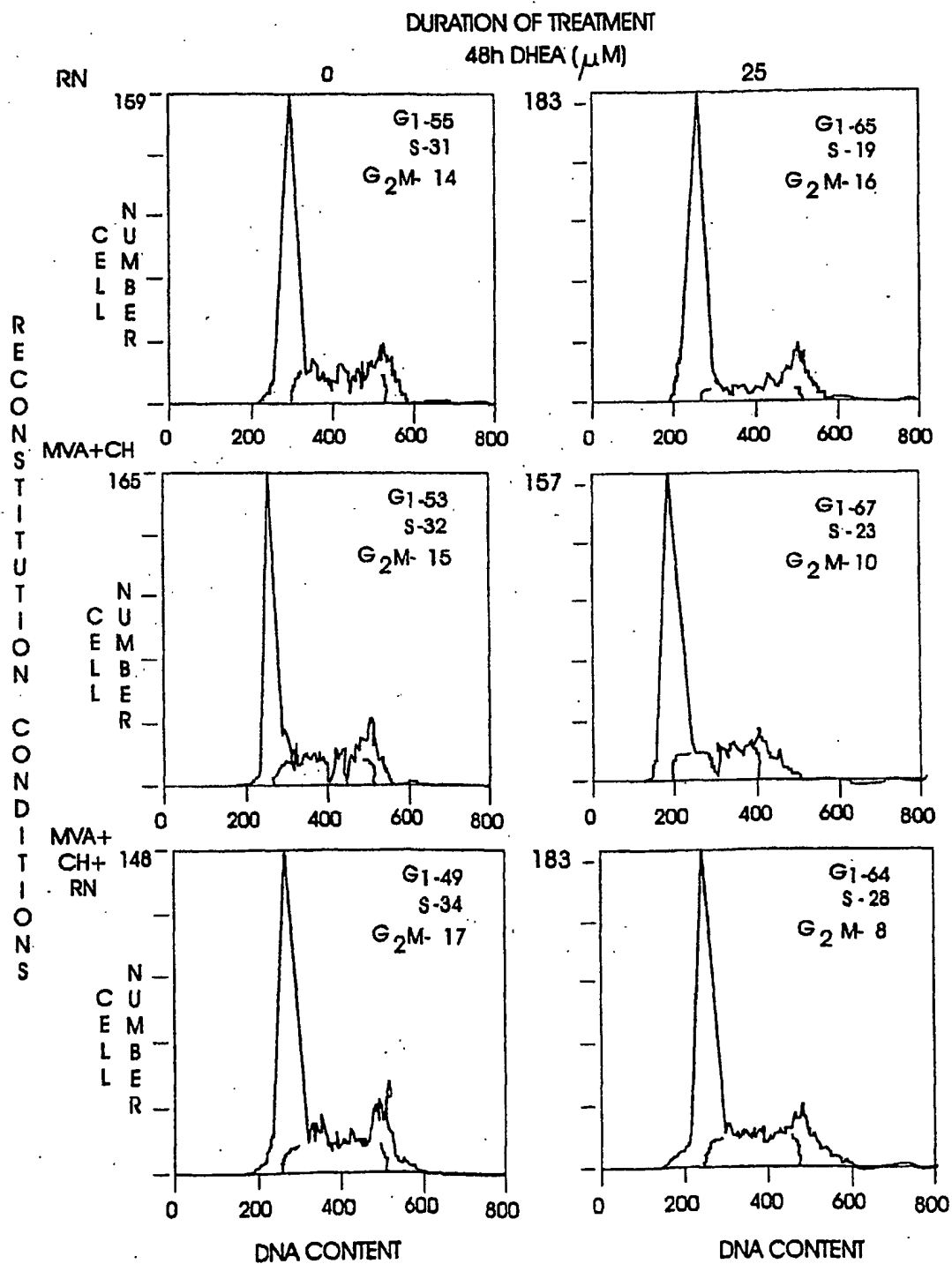




FIG. 4D

